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An Introduction to the History of Carcinoma of the Cervix Uteri[1]

EDWARD HOLMAN SKINNER, M.D.

Kansas City, Mo.

A REVIEW OF THE methods employed for the management of carcinoma of the uterine cervix in the pre-radiation era may seem like a vain and comparatively useless topic in this harassing period of global warfare, when many of our colleagues are in the armed forces and the rest of us are carrying an increased burden of civilian practice and straining to erect civilian defense.

There have been several attempts, and excellent ones, in medical literature that almost recite the story that is suggested by my title. Jameson *almost* tells it in the Clio Medica series in a history of gynecology and obstetrics (1). Mathieu recites the history of hysterectomy in a splendid source article in the *Western Journal of Surgery, Obstetrics, and Gynecology* (2). Kennedy (3) amplifies the record with a 1942 review of vaginal hysterectomy, his book being both an argument and a history eulogizing the famous Joe Price of Philadelphia. Stacey, in a paper presented before the Congress of Radiology, in 1937 (4) records the evolution of the treatment of fibromyomata of the uterus.

Naturally, the history of carcinoma of the cervix is a part of the history of cancer. Haagensen (5) gives an account of a most comprehensive exhibit of the rarities of cancer literature and illustration which he arranged for the Graduate Fortnight on Tumors held at the New York Academy of Medicine in 1932. Sifting these items and innumerable others, it is simple to see that our present-day concept of carcinoma of the cervix uteri is a product of comparatively recent knowledge. The more successful methods of treatment, such as will be discussed in this Symposium, are of even more recent times.

It would be easy to disregard the historical record of the centuries preceding the one in which we live, but it is interesting to follow certain historical stepping stones. Haagensen chose to divide the evolution of the knowledge of cancer into three epochs: the Epoch of Empiricism, from earliest times to 1761 A.D.; the Epoch of Description and Classification, from 1761 to 1900; the Epoch of Experimental Study, beginning in 1900.

The first of these, the epoch of Empiricism, included Egyptian civilization, the Hippocratic descriptions and the inadequate and useless ideas of Celsus, Galen, and the School of Salerno. Even the recorded vaginal hysterectomies for protruding uteri are barely pertinent to this discussion for, as is true today, the uterus exposed by procidentia or inversion rarely exhibited malignant growth.

The real starting point of the story falls in 1761, when Morgagni described the au-

[1] Presented, as part of a Symposium on Carcinoma of the Cervix Uteri, before the Radiological Society of North America, at the Twenty-eighth Annual Meeting, Chicago, Ill., Nov. 30–Dec. 4, 1942.

topsy findings in cancer of the uterus. He had, however, no idea of metastasis. It was Peyrilhe, in 1776, who provided the first intimation of extension *via* the lymphatics. It is interesting to observe that Peyrilhe's views were set forth in a thesis provoked by a prize offer. Similarly, one of the first planned and successful vaginal hysterectomies, by Langenbeck in 1813, was based upon a prize-winning essay by the Viennese, Wrisberg, delivered in 1810. An excellent anecdote concerning the Langenbeck operation relates that the elder Langenbeck began the operation with an arthritic assistant, who, when it came time to apply the ligatures upon the broad ligament, lay down on the job; thus deserted, Langenbeck, holding the stump of the broad ligament in one hand, was forced to throw a ligature around with the other hand and then pull the knot by holding one end of the ligature in his teeth. This scene has never been caricatured to my knowledge.

The important stepping stone to our present conception of carcinoma of the cervix is Wagner's *Der Gebärmutterkrebs* (1858), in which he described the metastatic pathways, though holding that the origins of the disease were to be found in connective tissue as well as in the epithelium. Virchow echoed these views in his monumental *Cellularpathologie*, appearing in the same year. From this time on, important events occur in increasing tempo. Thiersch in 1865 proved the epithelial origin of carcinoma, while Waldeyer extended this proof to include adenocarcinoma arising from glandular epithelium and demonstrated the hematogenous as well as lymphatic dissemination of cancerous growth.

During all this period of about 100 years there is a concomitant record of vaginal hysterectomy. Mathieu and Jameson, whose historical articles have been cited, avoid any particular or complimetary references to vaginal hysterectomy. Kennedy's anecdotal and pictorial record (1942) spurns any favorable reference to abdominal hysterectomy, though with others he agrees that Freund's presentation of the principles of this procedure, in 1878, is an historical landmark. From this point the several historical trails diverge until they meet again in our present irradiation era.

It is significant that the mortality attendant upon the wave of abdominal hysterectomies following Freund's publication provoked resolutions of condemnation by medical societies. Czerny again advocated vaginal hysterectomy and Joe Price of Philadelphia is said to have completed 4,000 such operations with a too, too unbelievably low mortality. Then came the late Howard Kelly, in 1888, with an aseptic, modern surgical technic with his successive accessible side and uterus-splitting operation. With a burst of enthusiasm, gynecologists proceeded to delete the pelvis from the general surgeon's field. No operating gynecologist would consider scratching out the uterus via the birth canal when rubber gloves, autoclaves, and bright lights permitted him such abdominal liberty and glamour.

We must not omit mention, as among those present in the immediate pre-irradiation era, of one Wertheim, who offered a theoretically successful operation for carcinoma of the cervix. It was just too difficult, however, for general distribution and was better limited to earlier stages of this disease.

We now enter upon a desperately competitive era in cancer history: an era of research; pathological studies; irradiation; surgical liberties, tempered only by mortality; surgical advances, impeded by unpleasant morbidity statistics; anesthetic progress; increased hospitalization, and most important, a public response to lay education and increasing support of research activity. This twentieth century has completely eclipsed the preceding centuries.

Significant events of interest in the first decade, aside from the waning Wertheim operation, was the promise of irradiation as foreshadowed by Foveau de Cormelles in 1904, when he checked menopausal

bleeding of benign origin by roentgen therapy, and the discovery by Chéron and Wickham and Degrais that the stem of radium in the uterus was equally potent, even causing regression of carcinoma of the cervix. It is at this point that one Dominici enters the picture, a vagabond type of pathologist with a genius for research in tissue changes incident to irradiation. His imagination led him to attempt filtration, and from his studies dates the progress of interstitial and intra-cavitary radium therapy.

It is easy to agree with Haagensen that the turning point from surgery to irradiation is the 1913 meeting of the German Gynecological Society, for it was here that Bumm, Döderlein, and Krönig and Gauss put the stamp of clinical approval and experience upon the preliminary studies by the Frenchmen named above.

During this period, in America, Abbe had been promoting radium therapy in a dignified manner. Then the irrepressible Kelly and his calmer consort, Burnam, startled the profession with their 1914 and 1915 presentations upon fibroids and cervical carcinoma, at successive yearly meetings of the American Medical Association. About this time Ewing came to the Memorial Hospital, New York, to amplify the clinical efforts of Janeway, Quick, Bailey, and Healy and give generous pathological support to irradiation therapy. Clark and Norris of Philadelphia added useful experience, and the prolific Schmitz in Chicago took the message to the West by translating the original work of Krönig and Gauss.

We must not neglect two interesting sidelights that x-irradiation dimmed aborning: the Percy cautery and Gellhorn's acetone cauterization of cervical carcinoma. These are historical items of certain value that the present glory of irradiation may not forever eclipse.

The influences of the Stockholm and the French Schools are not to be overlooked. Stockholm provided the statistics and Paris promoted the conservatism that have been healthy deterrents to rotarian demands for bigger, better, and swifter dosage factors.

Any historical review, even as sketchy as this, must not pass over the possibility that a simple, low-mortality operation such as vaginal hysterectomy at the end of the child-bearing period may have escaped its true destiny. Let us remind ourselves that squamous epidermoid carcinoma of the cervix originates within the very anatomical structure that vaginal hysterectomy deletes. The operation is as simple as an appendectomy and far simpler than a cholecystectomy. But while both these operations remove terminal pathology, a vaginal hysterectomy removes tissues which are capable of harboring a disease of high lethal qualities, in spite of the promises of irradiation.

1532 Professional Bldg.
Kansas City, Mo.

REFERENCES

1. JAMESON, E. M.: Gynecology and Obstetrics. Vol. 17, Clio Medica Series. New York, Paul B. Hoeber, Inc., 1936.
2. MATHIEU, A.: History of Hysterectomy. West, J. Surg. **42:** 1–13, January 1934.
3. KENNEDY, J. W., AND CAMPBELL, A. D.: Vaginal Hysterectomy. Philadelphia, F. A. Davis & Co., 1942.
4. STACEY, LEDA J.: Treatment of Uterine Fibromyomas. Radiology **22:** 212–218, February 1934.
5. HAAGENSEN, C. D.: An Exhibit of Important Books, Papers, and Memorabilia Illustrating the Evolution of the Knowledge of Cancer. Am. J. Cancer **18:** 42–126, May 1933.

Experiences in the Treatment of Carcinoma of the Cervix Uteri[1]

LEWIS C. SCHEFFEY, M.D.

Professor of Gynecology, Jefferson Medical College; Attending Gynecologist, Jefferson Medical College Hospital, Philadelphia, Penna.

THIS PRESENTATION relates to the management, treatment, and end-results observed in a group of patients with carcinoma of the cervix uteri encountered on the Gynecological Ward Service at the Jefferson Medical College Hospital during the past two decades. More specifically it represents a follow-up study of the patients seen and treated between Sept. 1, 1921, and Sept. 1, 1937. Thus a sixteen-year survey is made available, showing both the present-day and the five-year survival rates obtained during that period of time. Five, ten, and fifteen year reports of our work have been published previously (1, 2, 3). Opportunity for organizing and developing this clinic was afforded by the writer's former chief, Dr. Brooke M. Anspach, Consulting Gynecologist and Emeritus Professor of Gynecology at Jefferson.

The radium employed by the Department of Gynecology is supplied by the Lucy B. Henderson Radium Foundation, of which Dr. William S. Newcomet is Director. The x-ray therapy is administered by and in close co-operation with the Department of Roentgenology, of which Dr. Karl Kornblum is Chief. Reliance upon these sources of assistance is gratefully acknowledged.

PATIENTS OBSERVED AND FOLLOW-UP

Table I is self-explanatory. Seventeen patients were untreated, for various reasons. Nine presented disease so far advanced that no treatment was deemed advisable. Seven signed releases, and 3 of these were subsequently treated elsewhere. One patient, previously treated in a distant city, required no further treatment when she entered our clinic for observation.

TABLE I: PATIENTS OBSERVED AND FOLLOW-UP, 1921–37

	Total	Follow-up	Per cent
Patients seen	310	304	98.0
Patients treated	293	289	98.6

Six patients are untraced. Two, with advanced disease, were untreated; 3, with advanced disease, were treated, and all of these 5 patients are very probably dead. The sixth patient was alive and in good health when lost sight of eight years after treatment. The relatively high percentage of traced patients is the result of persistent and approved follow-up methods. These include personal attendance at the weekly Follow-up Clinic by the attending chiefs, an appointment system, contact by correspondence, visits by social workers, and co-operation of relatives and family physicians.

EXTENT OF INVOLVEMENT

The classification of the extent of disease, as proposed by the late Henry Schmitz, has been consistently followed ever since the establishment of the clinic. For practical purposes we consider it much more satisfactory than the relatively recent classification of the League of Nations, with the numerous subdivisions detailed in the published *Atlas* of the latter authority. The personal equation can never be entirely eliminated from any system of physical examination, but the probability of error is perhaps reduced when a less complicated scheme is consistently followed. The group to which a patient is assigned when first seen is maintained for the duration of her life. For instance, if a

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patient primarily classified as Group 3 shows marked regression of the lesion following treatment, we do not reclassify her as Group 2, on the assumption that the extent of the disease as first observed might have been of inflammatory origin, for if such a procedure were followed repeatedly, confusion would surely result. If reactivation of a lesion occurs after primary treatment, and further therapy is given, the initial classification is unchanged. Group 5 includes those patients seen with recurrent or unarrested disease whose primary treatment has been received elsewhere, either irradiation, surgery, or a combination of both.

TABLE II: EXTENT OF INVOLVEMENT (SCHMITZ CLASSIFICATION)

Group 1	6 cases	1.9%
Group 2	32 cases	10.3%
Group 3	226 cases	72.9%
Group 4	25 cases	8.0%
Group 5	21 cases	6.7%

The striking feature brought out by Table II is that 12.2 per cent of the cases observed have been classified as early (Groups 1 and 2), and this figure differs but little from that noted in previous reports of our work. This discouraging figure calls for continued diligence in the campaign for prophylaxis and prompt diagnosis, for, in our experience at least, truly early cases are comparatively rare. On the other hand, it is entirely probable that errors in clinical judgment may classify patients as Group 3 that more properly belong in Group 2, for parametrial induration and even fixation may represent inflammatory change rather than malignant extension. Possibilities such as this may give rise, as has been noted, to the controversial problem of reclassification of the lesion as primarily noted.

AGE INCIDENCE, PARITY, RACE

Because the majority of cases of cervical carcinoma occur during the menopausal era and afterward, physicians o ten lose sight of the fact that the disease is relatively frequent during the earlier decades of life. This fact is strikingly depicted in Table III, for 27 per cent of our patients were under forty years of age when first seen. Discounting this possibility is often responsible for the loss of valuable time in making an early diagnosis and instituting treatment promptly, omissions not infrequently noted in our experience. The occurrence of cervical carcinoma in a twenty-two-month-old infant is especially worthy of note.

TABLE III: AGE INCIDENCE, PARITY, RACE

Decade	Number	Per cent
1–9	1	0.3
10–19	0	0.0
20–29	11	3.5
30–39	72	23.2
40–49	91	29.3
50–59	86	27.4
60–69	44	14.1
70–79	4	1.2
80–89	1	0.3
Youngest, 22 months. Oldest, 84 years.		
27 per cent under age of 40		
Nulliparas	26	8.3
Negroes	31	10.0
Jewish	4	1.2

RESULTS OF TREATMENT

We have frequently commented upon the fact, as have many others, that freedom from signs and symptoms of cervical carcinoma for a period of five years following treatment is in no sense a criterion of "cure." We have seen recurrence as late as ten years after the initial treatment; for that reason we prefer to use the term "salvage" when speaking of patients who have survived for five years or longer after therapy. On the other hand, in our experience, prolongation of life for five years and longer has not infrequently resulted from the successful repetition of irradiation for recurrence or reactivation (4).

Our statistics therefore are presented on the following basis:

Present-Day Salvage: (*a*) The number of patients alive following treatment when the observation period is reported, based on the total number of patients actually seen (absolute per cent).

(*b*) The number of patients alive following treatment when the observation period is reported, based on the number

of patients actually treated (relative per cent).

Five-Year Salvage: The added number of patients treated during the observation period who have survived for five years or longer but have eventually died of carcinoma, of an intercurrent condition or, as in some instances, of an entirely different malignant growth (relative five-year per cent). Some patients in this category most certainly do not die of their original carcinoma, but this cannot be definitely stated unless proved by autopsy. It is unwise, therefore, to include such persons as actually salvaged carcinoma patients, though attention may properly be called to the fact that in this group a certain number presumably did not die as a result of their initial malignant growth. All untraced patients are regarded as dead.

TABLE IV: GENERAL RESULTS OF TREATMENT, ALL GROUPS

Of 310 patients observed, 44 are alive from 5 to 21 years	14.3 per cent (absolute)
Of 293 patients treated, 44 are alive from 5 to 21 years	15.0 per cent (relative)
26 additional patients survived from 5 to 17 years after treatment, establishing a total 5-year salvage of 70 patients	23.8 per cent (relative)
Primary mortality (4 patients)	1.3 per cent

Table IV presents the general results secured in the treatment of all patients, irrespective of the stage of the disease, and including all plans of therapy. An interesting fact that we have noted is that the number of patients surviving who were forty years of age or older when initial therapy was instituted is about twice as great as the corresponding number of survivors under that age. In other words, patients of the older group have done twice as well as regards survival as have those of the younger group.

Six years ago we reported an absolute salvage of 19.2 per cent, a relative salvage of 20.5 per cent, and a relative five-year salvage of 25.3 per cent. Eleven years ago the corresponding percentages were 14.2, 15.7, and 20.7 per cent, respectively.

Four patients died primarily as a result of treatment, a mortality of 1.3 per cent. Autopsy was performed in each case. In two instances pelvic peritonitis developed promptly, with death occurring on the seventh and tenth postoperative day, respectively. These women were between forty and fifty years of age and the postmortem examinations revealed pyogenic processes in the uterus and adnexa in addition to acute suppurative pelvic peritonitis. Radium therapy was undoubtedly a factor in producing or at least activating virulent pelvic infection. The other two deaths occurred in older women, fifty-four and sixty-four years of age. One died on the eighth postoperative day, the other on the twenty-first. In neither was peritonitis found at autopsy. Both exhibited advanced cardiovascular and renal disease in addition to the pelvic findings of advanced carcinoma. Consequently, these fatalities could scarcely be ascribed to the radium applications. Specific experience with pelvic peritonitis resultant from radium therapy has been detailed in a previous presentation (5). It may be stated that even the most careful preoperative care and preparation cannot wholly exclude the possibility of the development of post-irradiation peritonitis with potential fatality.

In Table V are shown the results of treatment, tabulated according to the extent of the disease, and grouped accordingly. The results secured in the "early cases" (Groups 1 and 2) are obviously the best. The ratio of success of treatment in Groups 1, 2, and 3 is roughly in the proportion of 4:2:1

The causes of death of those patients who survived their initial treatment for cervical carcinoma from 5 to 17 years —a total of 26—were as follows: cervical carcinoma, in 15 patients, five to ten years after treatment; gastric carcinoma, 1 patient, seventeen years after treatment; ovarian carcinoma, 1 patient, fifteen years after treatment; granulosa-cell tumor of the ovary, 1 patient, eleven years after treatment; diabetes, 2 patients, seven

TABLE V: RESULTS OF TREATMENT, ACCORDING TO GROUPS

Group	Patients Seen	Patients Treated	Alive 5-21 Years	Absolute Salvage (Per cent)	Relative Salvage (Per cent)	Total Relative 5-Year Salvage Patients	Total Relative 5-Year Salvage (Per cent)
1	6	6	3	50.0	50.0	4	66.6
2	32	32	9	28.1	28.1	14	43.7
3	226	221	29	12.8	13.1	49	22.1
4	25	15	0	0.0	0.0	0	0.0
5	21	19	3	14.2	15.7	3	15.7
Total	310	293	44	14.3	15.0	70	23.8

Groups 1 and 2 combined, 38 patients:
12 patients alive 5 to 21 years (31.5 per cent)
6 additional patients lived 6 to 12 years, increasing the relative 5-year salvage to 47.3 per cent

and fifteen years after treatment; cardiorenal disease, 5 patients, ten to sixteen years after treatment. One patient was untraced but is known to have been well at eight years. Of the patients dying from recurrence or reactivation of the original lesion, 4 survived from nine to twelve years after primary treatment; 2 were in Group 2 and 2 in Group 3. The occurrence of new malignant lesions elsewhere in 3 patients eleven, fifteen, and seventeen years after primary treatment for cervical carcinoma is of decided interest. It should be stated that the causes of death of 7 patients recorded as having succumbed to intercurrent disease from seven to sixteen years after successful treatment of cervical carcinoma were not all verified by autopsy but were reported as indicated by the attending physicians. This evidence must, therefore, be regarded as largely presumptive, although at death the ages of the patients ranged from fifty-six to eighty-one years.

TREATMENT WITH SURGERY AND IRRADIATION

Surgery was a factor in the treatment of but 8 patients. Four of these were treated primarily by us, between 1921 and 1923. Immediate panhysterectomy was carried out in 2 patients in Group 1, one of whom received preliminary irradiation with radium. In one recurrence in the vaginal vault followed three years later, irradiation with radium and x-ray was successful, and the patient has now survived for twenty-one years. The other died nine months after operation. Two patients in Group 2 received preliminary irradiation with radium, followed by panhysterectomy and subsequent irradiation; one died of recurrence in one and one-half years; the other survived for six years.

Four patients had been treated by primary panhysterectomy elsewhere, and they were accordingly placed in Group 5. None received preliminary irradiation as far as we know. Three of them treated by us, 2 with radium and one with x-ray for vaginal vault recurrence within a year of the primary operation, survived less than a year. The fourth patient, treated with both radium and x-ray, is now alive after eleven years (Table VI).

TABLE VI: TREATMENT WITH SURGERY AND IRRADIATION, 8 PATIENTS

Group	Patients	Preliminary Irradiation	Operation	Subsequent Irradiation	Alive	Relative Salvage (Per cent)
1	2	1, yes; 1, no	comp. hyst.	yes	1	50
2	2	yes	comp. hyst.	yes	0	0
5	4	no	comp. hyst.	yes	1	25
Total	8				2	25

Thus no patient was treated solely by surgery. The very prompt recurrence noted in each instance is mute evidence of the inadequacy of the operative procedures performed on these patients, or of faulty

indication for their employment. It was probably not the type of surgery of which men of the ability of Lynch or Bonney are capable, and serves to stress the point that if a surgical decision is made, it must be carried out by one qualified to perform a truly radical operation based on the premise of an undoubtedly early lesion. In a recent presentation we have gone into much detail regarding the disappointing role of inadequate and ill-advised surgery in the treatment of cervical carcinoma (6).

TREATMENT WITH IRRADIATION ONLY

Irradiation was used solely in the treatment of 285 patients. The results are set forth in Table VII. In percentage figures, they differ but little from those shown in Table V, with the exception of the results in the Group 1 patients. The relatively few patients in whom surgery was a factor in treatment accounts for the close approximation of the end-results.

TABLE VII: TREATMENT, IRRADIATION ONLY, 285 PATIENTS

Group	Patients	Alive	Rel. Salvage (Per cent)	Total 5-Year Patients	Relative Salvage (Per cent)
1	4	2	50.0	3	75.0
2	30	9	30.0	13	43.3
3	221	29	13.1	49	22.1
4	15	0	0.0	0	0.0
5	15	2	13.3	2	13.3
Total	285	42	14.7	67	23.5

Groups 1 and 2 combined, 34 patients:
11 patients alive 5 to 20 years (32.3 per cent)
5 additional patients lived 7 to 12 years, increasing the relative 5-year salvage to 47.0 per cent

Of more interest is the manner of employment of irradiation therapy and the results achieved thereby. During the observation period upon which this report is based, treatment underwent several changes. From 1921 to 1931 radium was used principally, most often as a single primary application. External irradiation with the x-ray was employed more or less sporadically during this time, subsequent to the local use of radium, and most often in instances of recurrence. From 1931 to 1934, roentgen irradiation was used much more frequently and systematically, subsequent to the radium applications, and as a regular plan of therapy. During this time, too, the x-rays were used more widely in far advanced cases, with the exclusion of radium. In 1934 and 1935 external irradiation first began to be used regularly as a preliminary procedure and 12 patients were so treated, while 10 received x-ray therapy both before and after the use of radium during this time. Since 1936, preliminary external irradiation has been instituted as a routine procedure of choice in most instances, and this plan is in vogue at present. This report is thus based on an observation period of sixteen years, during which radium was generally used primarily and x-ray therapy was utilized afterward as a supplemental factor in the majority of the patients treated prior to 1934–35, when preliminary x-ray irradiation began to be used.

Table VIII presents the various measures of radiation therapy employed and shows the number of patients treated by each plan, together with the contrasted present-day and five-year salvage. No attempt has been made to indicate the effect of the different forms of treatment upon each clinical group, as there were relatively few patients in Groups 1 and 2. It will be noted that those patients receiving preliminary external irradiation show a higher salvage rate, but it must be remembered that this rate includes the patients who were treated more recently by this method. Only when another five-year observation period has elapsed can we evaluate this altered technic with greater accuracy.

The influence of re-irradiation for recurrence is indicated by a study of 42 patients alive of 285 treated. Twenty-seven (64.2 per cent) are alive from five to nineteen years without evidence of recurrence following a single course of irradiation therapy, a relative salvage of 9.4 per cent. Fifteen patients (35.7 per cent) are alive from five to nineteen years because of re-irradiation during the ob-

TABLE VIII: TYPE OF IRRADIATION THERAPY AND RESULTS

Irradiation	Patients	Alive	Relative Salvage (Per cent)	Total Relative 5-Year Salvage Patients	(Per cent)
Single radium	117	19	16.2	31	26.4
Repeated radium	22	3	13.6	6	27.2
X-ray only	35	1	2.8	1	2.8
X-ray and radium	111	19	17.1	29	26.1
X-ray subsequent to radium	79	11	13.9	20	25.3
X-ray preliminary to radium	20	6	30.0	6	30.0
X-ray both before and after radium	12	2	16.6	3	25.0

servation period, thus increasing the relative salvage to 14.7 per cent. It has been argued by some that successful irradiation for recurrence means that the primary dosage was inadequate, but such an assumption is difficult to prove. The fact of the matter is that a goodly proportion of our surviving patients are alive today, or lived much longer, because of prompt retreatment when indicated. Early recognition of recurrence and immediate treatment depend upon a regular, systematic, and thorough follow-up service.

CARCINOMA OF THE CERVICAL STUMP

Among 310 patients, carcinoma of the cervical stump was encountered 16 times, an incidence of 5.1 per cent. This includes all patients seen, irrespective of when the supravaginal hysterectomy had been performed. The time period varied from one to twenty-five years. Five of the patients have survived treatment from five to fourteen years, a present-day salvage of 31.2 per cent, while 3 additional patients survived six, nine, and eleven years, respectively, indicating a relative five-year salvage of 50 per cent. Two of the latter patients died of recurrent carcinoma; the third, who survived eleven years, presumably died of a malignant granulosa-cell carcinoma of the ovary that was discovered ten years after primary treatment for carcinoma of the cervical stump. She survived operation one year. General discussion relative to the occurrence and prevention of cervical stump carcinoma is not pertinent to this report, other than to note the fact that the results of treatment have been better than with carcinoma of the cervix in general. Our views relative to the occurrence and possible avoidance of this condition, together with management, have been expressed in previous presentations (7, 8).

CERVICAL CARCINOMA SUBSEQUENT TO IRRADIATION FOR BENIGN CONDITIONS

A group of 7 patients with cervical carcinoma (1.6 per cent of 434 seen in 1921–42) had previously received irradiation for benign conditions of the uterus. The question of the occurrence of uterine cancer some time after the employment of radium or x-ray to control bleeding associated with fibromyomata or so-called functional bleeding (metropathia hemorrhagica) has been discussed very fully in a recent paper before the American Gynecological Society (9). At that time we reported 7 such instances in which cervical malignancy had occurred, 12 cases of fundal carcinoma, and one of uterine sarcoma. In this presentation our remarks will be confined to the cervical cases reported in the communication mentioned.

All 7 patients were multiparae, ranging in age from forty-two to sixty-one years when the cervical carcinoma was diagnosed and treated. Radium had previously been used to treat fibromyomata in 4 of them and x-ray in a fifth. Two were previously treated with radium because of fibrosis uteri or so-called functional uterine bleeding (metropathia hemorrhagica). A plastic operation, polypectomy, and vaginal myomectomy were accompanying procedures in 3 patients, respectively, and diagnostic curettage had been performed in all the radium cases, but not in the one receiving

x-ray therapy. Cervical biopsy and cauterization were done in only one instance. The time intervening between the treatments for the benign condition and the discovery of the malignant growth was two, four, six, six, nine, nine, and eleven years, respectively.

An irradiation menopause was produced in five patients ranging in age from forty-three to fifty-two years at the time of the primary treatment. None was produced in two patients, aged thirty-five and forty years, respectively. The radium dosage employed was 1,200 mg. hr. in four instances, and 600 mg. hr. in two others. In the patient treated with x-ray, 1,800 r was administered to each of four external portals.

Squamous-cell carcinoma later developed in each instance. Clinically one patient was in Group 1, 2 were in Group 2, and 4 were in Group 3. There is no evidence in these cases to support a statement regarding the presence or absence of cervical cancer at the time of the initial irradiation with the possible exception of a single patient in whom the performance of biopsy accompanied diagnostic curettage. In this particular instance the pathologist regarded the lesion with suspicion and, even though the cervix had been cauterized, the warning should have been regarded more seriously and subsequent hysterectomy been performed. In 3 other patients with recorded cervical lesions biopsy should have been done and treatment instituted at the time of the initial irradiation. In 2 additional instances no note was made of the condition of the cervix and one of these patients received x-ray therapy without cervical study or diagnostic curettage. In the seventh patient of the series the cervix was described as intact when first seen. Four of the patients died about a year after treatment for the carcinoma; one survived more than four years, while 2 remain alive, one year and four years after treatment.

Errors of omission may be charged to the management of 6 of these patients when they were first seen. Interest was primarily centered on the fundal lesion. Diagnostic curettage was properly employed and fundal cancer excluded in all patients except the one in whom x-ray therapy was used. In only two patients was the cervix thought of in terms of potential cancer, and in one of these an excellent opportunity for prophylaxis was lost. In the other case, secondary biopsy of the cervical canal beyond an intact portio followed promptly when an area of squamous carcinoma was found in the curettings secured in the investigation of uterine bleeding that occurred six years after the primary radium treatment for fibrosis uteri.

There is no substantial evidence to show that irradiation therapy of the uterine fundus either retarded or accelerated the development of cervical cancer later on. The point that should be emphasized is this: whenever diagnostic curettage is indicated to exclude cancer the procedure should be accompanied by cervical biopsy as a matter of record, especially if any gross abnormality is apparent. Not only should biopsy specimens be obtained from the portio and everted mucosa, but the lower cervical canal should likewise be included. Whenever irradiation therapy, either with radium or with x-ray, is chosen for the treatment of fibromyomata, fibrosis uteri, or functional bleeding (metropathia hemorrhagica), thorough biopsy of the cervix and cervical canal, as well as diagnostic curettage of the endometrial cavity, should be an accompanying procedure. Only in this way will the presence of carcinoma anywhere in the uterus be brought to light and indicated adequate treatment be provided.

TECHNIC OF IRRADIATION

The transition from radium therapy alone to its association with external irradiation has been mentioned briefly in a preceding paragraph. The technic, with variations, is detailed as a matter of record.

Radium Application: During the observation period embodied in this report

(1921 to 1937), intracervical and interstitial radium applications were employed, with the use of (1) a 50-mg. capsule of radium, screened with 0.3 mm. of silver and 1.0 mm. of brass, enclosed in black rubber tubing of 2 mm. thickness, and placed in the cervical canal; (2) 8 needles, each containing 12.5 mg. of radium, screened with 0.3 mm. of Monel metal and generally inserted about the periphery of the growth. This combination totalled 150 mg. of radium, which was held in position with gauze packing for the time requisite to insure varying dosages. From 1921 to 1924 the average dosage was between 2,000 and 2,200 mg. hr.; from 1924 to 1927, it averaged 3,000 mg. hr.; during 1927 and 1928, the average was 4,300 mg. hr.; from 1928 to 1936 it was decreased to 3,600 mg. hr. because of many severe reactions. Beginning in 1935, an additional 50-mg. capsule, screened with 0.5 mm. of platinum, was obtained to replace the brass capsule or to use in conjunction with it. This armamentarium continued in consistent use until early in 1938, when three 50-mg. capsules screened with 1.5 mm. of platinum and ten 10-mg. needles screened with 0.5 mm. of platinum were secured to replace the former equipment. Another year of observation will have to elapse before we can determine what change in five-year results, if any, has resulted from this more recent alteration in screening.

X-ray Application: The late Dr. Willis F. Manges and his associates, Drs. J. T. Farrell, Jr., and R. Manges Smith, directed the technic of external irradiation throughout the period of time covered by this report. Since 1938 this phase of the treatment has been supervised by Dr. Karl Kornblum and his co-workers.

Prior to 1927 massive doses were given at a single sitting, at right angles to one of 3 or 4 pelvic ports. The amount given was that which the skin would tolerate, and the entire course was completed in three or four days. The factors were 3 ma. at 170 to 200 kv., filtered through 0.5 mm. of copper and 1.0 mm. of aluminum at 50 cm. skin-target distance, through ports 16, 19, or 20 cm. square. The total dosage delivered through each port varied from 800 r to 2,100 r measured in air.

After 1927 the fractional method was followed, treatment being directed through 4 ports, 2 anteriorly and 2 posteriorly, with the factors as previously mentioned. The object then was to deliver 100 per cent of the skin erythema dose into the depths of the pelvis in two weeks by giving treatment on alternate days until the saturation level was reached. Treatment was then continued for two more weeks. The total dosage delivered through each port by this method varied from 1,400 to 1,500 r. This plan was followed with but little variation throughout the remainder of the observation period embodied in this report.

Beginning in 1934–35 external irradiation was used more and more as a routine procedure prior to the application of radium. In 1938 and 1939, still with the same factors, multiple portals averaging four in number, two anteriorly and two posteriorly, continued to be employed, with cross-firing on the uterus and parametrium. Two such areas are treated daily, each receiving 200 r (measured in air). The treatments are continued until a well marked erythema is obtained, which in general will occur with a total of 1,600 to 2,400 r to each portal. Such a series requires about three weeks for completion.

When we began to use preliminary external irradiation, the radium was applied near the termination of the x-ray treatments or soon afterward. Now the radium application is delayed from three to four weeks, since reactions were sometimes too severe when the internal and external irradiation followed each other so closely. There is no doubt that the x-rays diminish local necrosis, slough, and infection; pain and bleeding are frequently relieved as well. On the other hand, if too long a time elapses before applying the radium, vaginal vault contractures may occur that render radium insertion difficult. It remains to be seen what the five-year results will be

with this present technic, but the trend of the three- and four-year survivals augurs well.

Since January 1942 transvaginal therapy has been used in conjunction with preliminary external irradiation and the local use of radium. Dosage through this portal averages 2,000 r. The apparently satisfactory results attained by Behney, Pendergrass, Bromer, Merritt and others using this method convinced us of its desirability.

HISTOLOGIC GRADING AND PROGNOSIS

We have no reason to change previously expressed views with regard to the impracticability of attaching prognostic significance to the histologic grading of carcinomatous lesions of the cervix. Radiosensitivity is relative and radiocurability is not an equivalent term. The response to irradiation is contingent not only upon the biologic processes that are constantly going on in all the tissues within range of treatment but also, to an appreciable extent, upon the age and physical status of the patient and the amount of irradiation administered. Consequently it is probable that prognosis depends to a far greater extent upon the clinical characteristics of the lesion and its subsequent response to irradiation than upon primary microscopic gradation. The majority of our surviving patients exhibited lesions of a low or intermediate grade of malignancy and patients with an anaplastic, highly malignant type of tumor cell frequently reacted badly to irradiation. Those with adenocarcinoma did relatively poorly.

COMMENT

It would be superfluous to present statistics relating to the appearance and duration of symptoms prior to treatment. Irregular vaginal bleeding, both pre- and postmenopausal, generally accompanied by discharge, has usually been present for periods of time ranging anywhere from a few months to a year and a half before carcinoma was eventually discovered and treated. Neither should it be necessary to repeat the familiar story of delay in investigation, for which the patient and the doctor alike must share responsibility; delay in diagnosis because of undue modesty, apprehension, lack of consultation, failure of adequate examination, and faulty selection of treatment. Too often abnormal bleeding is assumed to be of a functional nature and hormonal therapy is instituted without thorough pelvic investigation and elimination of organic disease. It must be conceded, however, that in exceptional instances cervical carcinoma may develop rapidly, and even extensively, without the occurrence of subjective or objective symptoms and signs. Hence the desirability of routine pelvic examinations with frequent biopsies is unchallenged. Catharine Macfarlane (10) and her group have shown what can be accomplished in this respect. The importance of prophylactic biopsy with cauterization or trachelectomy as indicated should be constantly stressed. In our own experience this has revealed unsuspected carcinoma in several instances.

Time and space will not permit discussion of numerous interesting problems peculiar to individual patients in this series, occurrences which perhaps are not an uncommon experience in any similar group. Some have been touched upon in passing, as the occurrence of multiple malignant lesions and the coincidental finding of pelvic inflammatory disease. Granulosa-cell tumors of the ovary were removed from 2 patients, ten years after successful radium therapy for cervical carcinoma. Inadequate or ill-advised surgical treatment has been decried. Cancer of the cervix occurring after irradiation of the uterus for benign conditions has been discussed in some detail. Coexistent syphilis is not infrequent. Odd metastases have been observed; annoying and destructive bladder and bowel lesions have been seen. Fistulas are known to have occurred in at least 12 per cent of our patients; how many more is problematical, as the exact circumstances attending deaths of patients in remote areas are not always clear.

SUMMARY

1. An analysis of a series of 310 patients with carcinoma of the cervix uteri observed on the Gynecological Ward Service, Jefferson Medical College Hospital, from Sept. 1, 1921, to Sept. 1, 1937, of whom 293 were treated, is presented, based upon a follow-up study of 98 per cent of the patients seen and of 98.6 per cent of those treated.

2. The absolute salvage rate of patients alive at the time of this report is 14.3 per cent. The relative rate is 15.0 per cent. The relative five-year salvage rate, including deceased patients who survived for five years or longer after treatment, is 23.8 per cent.

3. Pertinent data have been presented for analysis and discussion.

255 South 17th St.
Philadelphia, Penna.

REFERENCES

1. SCHEFFEY, L. C., AND THUDIUM, W. J.: Am. J. Obst. & Gynec. **22:** 247–254, August 1931.
2. SCHEFFEY, L. C., AND THUDIUM, W. J.: Am. J. Obst. & Gynec. **31:** 946–956, June 1936.
3. SCHEFFEY, L. C., THUDIUM, W. J., AND FARELL, D. M.: Am. J. Obst. & Gynec. **43:** 941–954, June 1942.
4. SCHEFFEY, L. C.: Am. J. Obst. & Gynec. **38:** 907–911, November 1939.
5. SCHEFFEY, L. C.: Am. J. Obst. & Gynec. **28:** 214–221, August 1934.
6. SCHEFFEY, L. C., AND HAHN, G. A.: Penna. M. J. (in course of publication).
7. SCHEFFEY, L. C.: J. A. M. A. **107:** 837–844, Sept. 12, 1936.
8. BEHNEY, C. A.: Am. J. Obst. & Gynec. **40:** 780–790, November 1940 (discussion).
9. SCHEFFEY, L. C.: Am. J. Obst. & Gynec. **44:** 925–951, December 1942.
10. MACFARLANE, C., FETTERMAN, F. S., AND STURGIS, M. C.: Am. J. Obst. & Gynec. **39:** 983–989, June 1940.

DISCUSSION

(Papers by E. H. Skinner and L. C. Scheffey)

Frederick W. O'Brien, M.D. (Boston, Mass.): I conclude that Doctor Scheffey probably has the same type of patient that we have at the Boston City Hospital. Reports of 85 per cent five-year cures in early cases, published by some, represent a different social grade of patient and frequently are based on a pathological diagnosis of carcinoma *in situ*.

Some believe that we should differentiate between the terms "cure" and "salvage." The word "cure" usually means that the patient is alive and well at the end of five years without evidence of disease, while the term "salvage" means that she is alive with evidence of disease.

I was glad to hear the reference to the work of Bonney. His results with hysterectomy are probably as good as can be found anywhere, yet he has to admit that surgery in cancer of the cervix has probably reached its peak and that radium and x-ray most probably can surpass it. He hopes that the Wertheim operation will not fall into disuse not because it is a cure for cancer but, he says, because, by doing it, one obtains a knowledge of the pelvis that is to be had in no other way.

For some years now patients at the Boston City Hospital have been treated with high-voltage irradiation before application of radium and at times we have had difficulty in dilating the cervix in preparation for radium insertion. I want to ask Doctor Scheffey whether or not he has had the same experience. It is possible that in our cases we wait too long.

The difficulty in making the radium application has not been due to the fact that a radiologist has attempted to do it, because in my hospital the radiologist merely prescribes the dosage and supervises the insertion of the radium, which is actually done by the gynecologist.

Doctor Scheffey is to be commended for his fearless statement of absolute and relative survival rates. I don't think we shall get anywhere in this matter of cure of cancer until we all adopt similar tactics. The selected groups do equally well with surgery or radiation. The important thing is what happens to the whole group. I would like to compliment Doctor Scheffey on an excellent presentation.

Herbert E. Schmitz, M.D. (Chicago, Ill.): I would like to emphasize one point brought out by Doctor Scheffey. In many of the large surgical clinics throughout the United States today, since the perfection of the technic of vaginal hysterectomy, the use of radium for benign bleeding in the menopause is being discarded. The reason given is that with simple vaginal hysterectomy the mortality rate is extremely low and that in uteri left *in situ* after radium treatment for benign lesions, the incidence of future malignant growth is high. In Doctor Scheffey's series there were only 7 patients among 434 who had received irradiation for benign lesions. I feel that this is an extremely important point.

Milton Friedman, Major, M.C. (New York, N. Y.): During the past decade, the anticipated improvement in cures of carcinoma of the cervix has not materialized. One of the explanations is the tendency for each clinic to standardize its radiation technic in the face of a lesion which presents varied clinical pictures.

I have two points in mind, which were broached by the previous speakers. The first one is: In at-

tempting to estimate the ideal daily tumor dose for a squamous-cell epithelioma between grade II and grade III, which represents the most usual type of carcinoma seen in the cervix, we have chosen a figure of approximately 275 roentgens per day. This is the average daily tumor dose delivered to carcinomata of the upper respiratory tract, which are successfully treated with fractionated external irradiation. When the daily tumor dose is much smaller than this optimum figure, the irradiation becomes inefficient; the amount of shrinkage from the external irradiation is small; there is early maturation of the tumor so that histologically it appears to be more differentiated; the tumor bed becomes more fibrous and less vascular; and finally, not only does the tumor itself become more radioresistant, but the tumor bed becomes less able to tolerate radiation. Such inadequate roentgen irradiation is commonly seen in obese women in whom the daily tumor dose from the external irradiation is inefficiently small. Commonly, after administering an inefficient course of external irradiation, there is an additional delay of one or two weeks before radium is inserted, and the undesirable results described above are aggravated. Therefore, the time-spacing of external irradiation as it affects the daily tumor dose and the time of radium insertion are consequential features.

The second point is: Each clinic tends to use one type of radium technic. The geometric configuration of carcinoma of the cervix is so varied that no single set of radium applicators is suitable for every case. One should have available a number of applicators: Curie colpostat and cork, metal tandem with attached single or double crossbar, tandem with ring, Paterson and Parker (Manchester) corks and tandems, Radiumhemmet boxes, separate foci for vaginal wall plaques, needles for interstitial irradiation of the outlying parametrium.

The principle of fractionated radium therapy is important and well repays the added effort required.

To summarize: Improved systems of roentgen and radium technic for the treatment of carcinoma of the cervix have been disappointing because of the failure to apply and modify these systems to fit the individual case.

Edward H. Skinner, M.D. (closing): I was interested in the comment of Doctor Schmitz, for I, also, was pleased with Doctor Scheffey's figure in regard to the incidence of cancer in patients who had received irradiation for a benign uterine condition. As I recall, 1.6 per cent of his series had received previous irradiation for benign disease. That is a very low figure.

Again, I was not surprised at all at the number of stump carcinomas among Doctor Scheffey's group. I feel quite sure that I have an even larger percentage. It is my idea that supravaginal hysterectomy is done at smaller hospitals throughout the country by those who may not be capable of doing either a vaginal hysterectomy or a panhysterectomy, and who fail to realize what they are working with before they operate.

The number of good results obtained in these stump carcinomas is surprising and the situation is hard to understand, but my own experience is similar to Doctor Scheffey's in this respect.

I am not at all alarmed about the evidence of competition between surgeons and radiologists in the treatment of cervical carcinoma. This will continue and there is no use trying to avoid it. It is one of the circumstances which may eventually serve to segregate those who are radiotherapists from those who are roentgen diagnosticians. This, I feel sure, is a reasonable division within radiology. It is embarrassing to be consulting with a surgeon upon a diagnostic problem while at the same time he hears the x-ray machine buzzing upon a patient upon whom he might have operated with equal authority.

Lewis C. Scheffey, M.D. (closing): First, I wish to thank those who have discussed this paper. It is always gratifying to have our colleagues speak freely about what has been presented.

In answer to Doctor O'Brien, I am really afraid to use the word "five-year cure" because every once in a while we see a patient pass the five-year mark with no visible evidence of disease and yet a year or two later show a recurrence. I have therefore chosen to use the word "salvage;" perhaps "survival" is a better term.

Doctor O'Brien also asked whether or not we had difficulties in inserting radium after external irradiation. Yes, we do. However, when we started to use the radium too soon after a course of x-ray therapy, it frequently seemed that the patient experienced a severe reaction. That is why we now wait anywhere from two to four weeks, and this is in line with what Doctor Friedman mentioned in his learned discussion of the physics of irradiation.

Doctor Schmitz commented upon the widespread idea that radium used for benign conditions may predispose to carcinoma later on. In a recent study presented before the American Gynecologic Society, I went into that question in detail both in respect to fundal cancer and cervical cancer. In no case did we find that radium had been at fault. When malignant growth developed subsequently, it was always due to some error of omission or faulty employment in the earlier management of the case. Irradiation *per se* played no part in it.

I agree with Doctor Skinner's pertinent remarks about the problem of carcinoma of the cervical stump. I believe that it could not occur if supravaginal hysterectomies were preceded by thorough study and adequate treatment of the cervix, and if the supravaginal cases were carefully followed up. Preferably, if the cervix is seriously diseased, a complete hysterectomy may be the better plan, especially in women over forty years of age.

Further Experience with Pneumoperitoneum as an Aid in Pelvic Irradiation[1]

L. R. SANTE, M.D.
St. Louis, Mo.

RADIATION THERAPY of any part or organ must always take into account the vulnerability of the intervening body tissues. This is especially true in irradiation of the pelvic organs for carcinoma of the cervix. In the past there has been ample evidence of the extreme radiosensitivity of the intestinal mucosa. Animal experiments (1–4) and some clinical reports (5) have attested to this fact. This sensitivity of the intestinal mucosa can readily be verified by including in the same field the intestinal mucosa of a colostomy and the adjacent surrounding skin. If this area is subjected to increasing doses of roentgen radiation, the intestinal mucosa will show a severe reaction, presenting congestion, edema, pseudo-membrane, and mucosal hemorrhages, following doses which produce only a moderate skin erythema. Clinically, this radiosensitivity of the intestines is manifested by colicky abdominal pains, diarrhea, rectal tenesmus, and passage of blood and mucus in the stools. Such reactions are most severe as a result of massive dose x-ray therapy; fortunately, with our present-day divided-dose technic, such reactions are rarely encountered.

There can be no doubt, however, concerning the desirability of introducing larger quantities of radiation into the pelvis in the treatment of cancer if vital normal structures can be safeguarded. Experience in the treatment of carcinoma of the cervix indicates this need only too clearly. Radiation therapy can satisfactorily destroy the local cervical lesion in most instances; it is the extension of the malignant disease into the parametrial regions which is most difficult to reach with adequate dosage.

The radiation from radium applicators in the cervical canal and vagina rapidly falls off due to the operation of the inverse-square law, so that an adequate lethal dose for carcinoma cells cannot be delivered except for a very short distance into the adnexal regions (6). Likewise, external roentgen radiation applied over these areas in woefully lacking.

For these reasons we were led to seek some method by which the radiation delivered into the adnexal regions could be increased. It appeared clear that if in some manner the intestines could be removed from the field of irradiation, greater quantities might be introduced with impunity.

Pack and Livingston (7) and others had recommended irradiation of the pelvis with the patient in the Trendelenburg position to cause as much upward displacement of the intestines as possible. There can be no doubt that this position does have a tendency to displace the intestines upward to some degree, but roentgenographic examination with the aid of barium will readily disclose that comparatively little change takes place and that the greater portion of the bowel still remains in the lower abdomen, overshadowing the pelvic structures. The forces of cohesion prevent complete emptying of the structures from the pelvis.

Obviously the abdominal cavity must be enlarged to give room for displacement of the intestines if this is to be satisfactorily accomplished. The possibility of artificial pneumoperitoneum for the purpose at once presented itself for consideration (8). The use of pneumoperitoneum for diagnosis of pelvic lesions left no doubt about the possibility of intestinal displacement by

[1] From the Department of Radiology of the St. Louis City Hospital. Presented, as part of a Symposium on Carcinoma of the Cervix Uteri, before the Radiological Society of North America, at the Twenty-eighth Annual Meeting, Chicago, Ill., Nov. 30–Dec. 4, 1942.

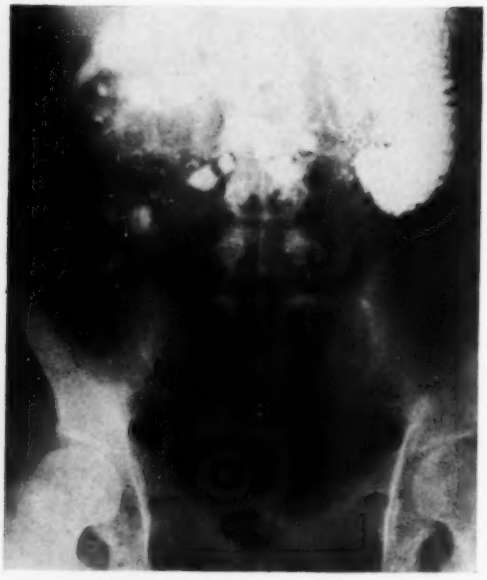


Fig. 1. With the patient in the Trendelenburg position after pneumoperitoneum, the air fills the pelvis, displacing the intestines into the abdomen. Postero-anterior projection.

this method (Fig. 1). We had tried it on a few patients a number of years earlier (1924), but the fixed position of the x-ray tubes in use at that time rendered the method too cumbersome to permit of its practical application. The versatility of present-day shock-proof tubes and equipment removed this difficulty, and rendered the procedure much more practical.

Recapitulation of the method of procedure previously described, with certain changes dictated by further experience with the method, seems advisable.

PROCEDURE

1. Produce Artificial Pneumoperitoneum: After evacuation of the intestinal tract, pneumoperitoneum is produced by a simple technic previously described (9). Inflation is carried to a point somewhat greater than that ordinarily used for diagnostic pneumoperitoneum. The patient should be kept on her back in bed for the first day or so, until she becomes accustomed to the presence of air in the abdomen. Pain in the back, between the shoulders, is the penalty of assuming the upright position during this time, but this subsides immediately when the patient again lies down. In most cases, after the second or third day she may be up and about. Air is used, since large amounts of this gas usually require from ten to fourteen days for complete absorption, often providing sufficient time for carrying out the entire course of roentgen therapy with a single filling. One refill, about the seventh day, is all that should be necessary under any circumstances. The widespread use of pneumoperitoneum in the treatment of pulmonary tuberculosis is evidence that air in the abdomen is well tolerated over long periods of time.

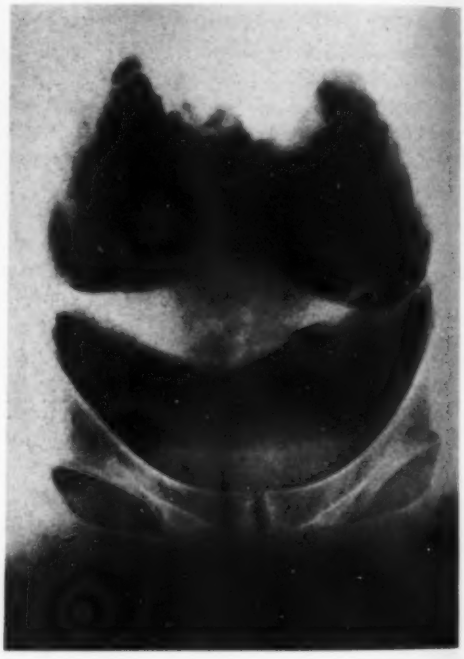


Fig. 2. Roentgenographic examination of the pelvis along the pelvic axis discloses the pelvic organs and often gives information as to the degree of involvement, which is of value in treatment. The uterus is seen "on end" with tubes and ovaries on either side; the rectum posteriorly was left partially filled to indicate its position.

2. Make Roentgen Examination: With the patient lying on the abdomen, head downward, on a tilt table lowered to an

angle of about 45 to 50 degrees, the air rises to fill the pelvis, enveloping the pelvic organs and displacing the intestines. Roentgen examination of the pelvic organs (10) is made by projecting the roentgen-ray beam along the pelvic axis, represented roughly by a line between the anus and umbilicus. When the patient lies on the face, hips elevated to this degree, the roentgen-ray beam will be almost straight downward; when she lies on the back in the same tilted position, the beam must be directed downward to the feet, to a corresponding degree, in order to be projected along the pelvic axis.

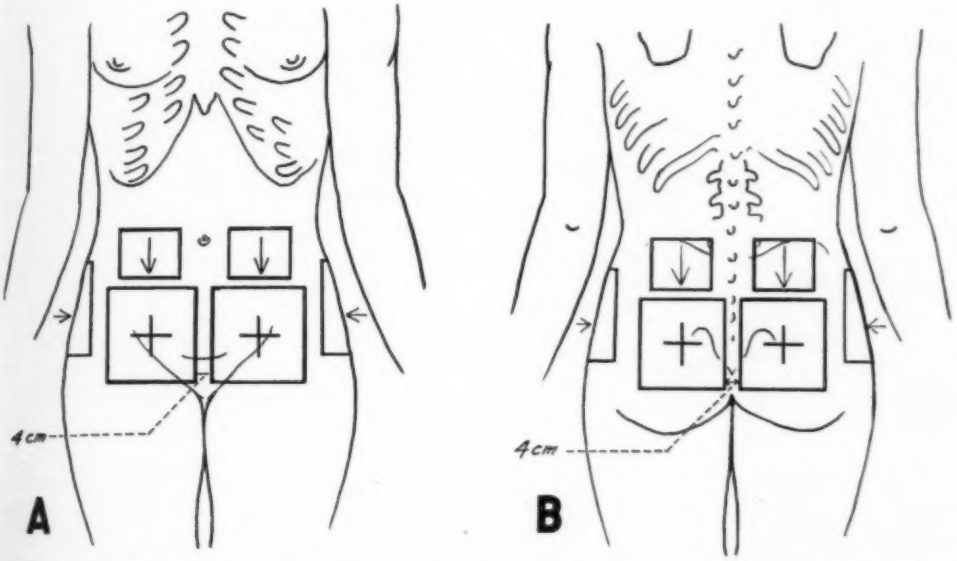


Fig. 3. A. Anterior portals. B. Posterior portals. Four ports are outlined with indelible pencil anteriorly and posteriorly, *with the patient in the Trendelenburg position;* otherwise the skin portals will be displaced when the inclined position is assumed for treatment.

The information received from this roentgen examination may be of value in treatment (Fig. 2). The facts to be determined are the presence, position, and size of the uterus and the location of the other pelvic organs. Any masses can be observed and their relationship to the uterus and other pelvic structures noted. It may not be possible, with certainty to determine the exact character of the pathologic condition. This examination will also determine whether the intestines have been completely displaced from the pelvic region and lower abdomen, or whether, as a result of adhesions or other cause, they remain firmly in place in spite of pneumoperitoneum and the inverted position.

3. Make Necessary Measurements: Necessary measurements are made, recording the thickness of the body in the antero-posterior direction and along the pelvic axis, with the patient lying on her face as well as on her back. The contour of the body at the level of the cervix is recorded by using a flexible lead strip or a physicist's variable curve.

4. Outline the Portals for Roentgen Therapy: The portals for roentgen therapy are outlined with the patient in the same inverted position in which treatment is to be carried out (Fig. 3), four portals being used anteriorly, two on each side, and four portals posteriorly, likewise two on each side, covering very closely the areas recommended by Arneson and Quimby (11). The size of the lower portals should be

15 × 15 cm. or 10 × 10 cm., depending upon the size of the patient, with the roentgen-ray beam directed straight inward into the pelvis. The size of the upper portals should be 10 × 10 cm., with the roentgen-ray beam directed downward along the axis of the pelvis. It has been found advantageous to separate all fields 4 cm. in the mid-line and to incline the beams straight inward eliminating the slight tilt toward the mid-line. Two additional lateral portals, 10 × 15 cm., will add to the parametrial dosage. In

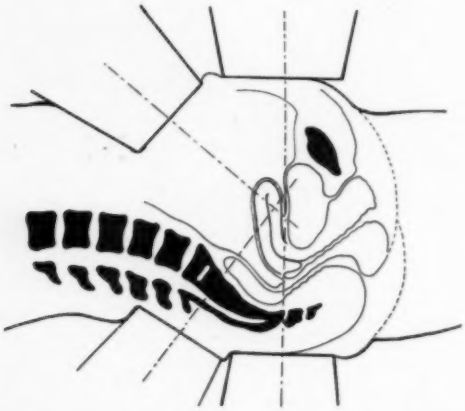


Fig. 4. With this arrangement a cross-fire effect is produced on the adnexal regions on both sides, with the least amount of radiation expended on the mid-line structures from external sources.

this way at least four portals will be directed over each adnexal region from the anterior and posterior directions, and one laterally. Anteriorly on either side the lower portals should be located with their lower edges just below the upper margin of the symphysis pubis and the roentgen-ray beam should be directed perpendicularly straight through into the pelvis; the upper portals should be marked out just above, and in this case the beam should be projected obliquely downward along the pelvic axis. This is the portal in which deep compression may be most effectually used. A bakelite cap made of material not more than 2 mm. thick may be fitted over the cone to permit compression more effectually. Posteriorly four fields, two on either side, should be laid out also, 10 × 10 cm., or 15 × 15 cm., depending on the size of the patient; in this case the lower fields will be at the same level as the corresponding anterior fields, with the lower edges just below the level of the coccyx, with the roentgen-ray beam directed perpendicularly inward. The second set of fields, just above these, should have the beam projected downward toward the adnexal region.

Projection of a roentgen-ray beam along the pelvic axis with a patient in the prone position requires direct exposure of the vulva, and this should be avoided. In all external irradiation the vulva is protected by a bag containing equal parts of fuller's earth and china clay, held firmly between the thighs. Lateral fields exposed on either side will add materially to the dosage delivered to the parametrium.

5. Accurately Locate the Portals and Determine the Optimum Direction of the Roentgen-Ray Beam in Each Case: The lower anterior and posterior fields are centered directly over the parametrium so that in these cases the beam should be directed perpendicular to the body. The direction of the beams for the upper fields can be determined in the following manner:

A small adjustable indicator rod consisting of a straight piece of steel wire about 4 inches long attached to a pliable metal base (a piece of $^1/_{16}$ inch sheet lead) is applied to the abdomen with adhesive or made sufficiently large that it will remain in place by its own weight, the base of the rod being centered at the middle of the medial margin of the portal. With the index finger of one hand in the vaginal fornix lateral to the cervix, sight *mentally* along the rod, varying the angle of the rod until it is directed toward the vaginal finger (8). This angle may be measured with relation to the table top by a protractor, and the direction of the beam for each portal can be determined in this manner for all subsequent treatments. This is an old method utilized by Holzknecht to determine the direction of the roentgen-ray beams for multiple por-

tals in cross-firing a tumor in the depth. It is sufficiently accurate for all practical purposes; indeed, extremely accurate cross-firing may be undesirable, since it may lead to too abrupt limitation of the field of irradiation. This arrangement in effect produces cross-firing of each adnexal region (Fig. 4).

6. In Setting up These Portals for Radiation Therapy, Take Due Advantage of Compression Wherever Possible: Even slight compression materially increases the depth dose.

7. Dosage Factors: We have utilized both 50 and 80 cm. distances, the latter in heavier patients because of the greater depth dose which it affords. With 200 kv., 18 ma., 1-mm. copper effective and 1-mm. aluminum filter, half-value layer of 1.46 copper, 49 r per minute is delivered until a dose of 200 r, measured in air, is administered to all four anterior areas and one lateral portal on a single day. The following day treatment is given through all four posterior portals and the other lateral portal. In this way both adnexal regions receive daily irradiation, whereas each skin portal receives irradiation on alternate days only. Treatment is continued until a pronounced skin reaction occurs; this usually progresses to desquamation. This was found to require about 2,000 r for a 15 × 15-cm. portal and 2,400 r for a 10 × 10-cm. portal.

The use of radium applicators in the uterus and in the vagina can be carried out just the same as if pneumoperitoneum had not been induced. In fact, it probably would be better to carry out this part of the treatment without pneumoperitoneum either before or after external x-radiation is applied.

The use of intravaginal cone radiation with x-rays to take the place of radium is a method having great potentialities for harm as well as for good, and it should be instituted very cautiously. There can be no doubt of its effectivness in destroying the local cervical lesion, but it is certainly of much less value in irradiation of the parametrial structures. The pronounced increase in depth dose produced by this method becomes a detriment if caution is not observed. In a previous publication we mentioned that we had administered by intravaginal cone (2.5 to 3-cm. field) as much as 1,000 r per treatment on ten successive days for ulcerating, less bulky growths, or for fifteen days for extremely large, bulky tumors of the cervix (using 200 kv., 1-mm. copper effective and 1-mm. aluminum filter, 50 cm. distance), but that *such large doses were probably not necessary or desirable.* As stated in our original publication, in our first series we confined this technic almost entirely to patients who refused the use of radium in treatment of carcinoma of the cervix; all other patients were treated with radium in the usual manner. About 75 per cent of the dose mentioned, or 750 r per treatment for ten successive days, was suggested as more desirable, but even this amount may not be free from danger. There can be no doubt that intravaginal treatment in this manner with x-rays alone can cause complete disappearance of carcinoma of the cervix. The cervix itself may resume a pink almost normal appearance with complete epithelialization, and yet the more sensitive rectum several centimeters beyond, through bulky uterine and malignant tissue, may be subjected to intolerable amounts of radiation. Obviously in patients who have received radium therapy any subsequent intra-

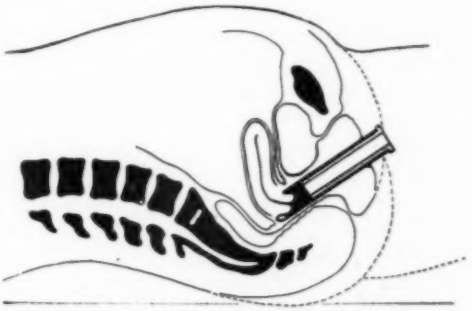


Fig. 5. The great difficulty with the use of the intravaginal cone for radiation treatment is the fact that the cone is directed in the mid-line toward the rectum.

vaginal x-ray therapy must be reduced in quantity.

One patient, almost a year after radiation therapy, developed a sharply demarcated defect in the rectal wall which suggested blood vessel thrombosis. The inability to shield the rectum and lower sigmoid from radiation by the intravaginal cone can easily be understood, since the cone is always directed toward the bowel (Fig. 5).

Perhaps the dosage and methods recommended by Merritt (12) and by Erskine, with a shorter tube distance if possible (it is difficult to work with shorter tubes in association with bulky shock-proof x-ray tubes) and with lower kilovoltages and less filter, but utilizing rigid connection for the vaginal cone and tube, might be more nearly ideal.

At any rate, the use of artificial pneumoperitoneum for the purpose of increasing the amount of radiation which can be introduced into the parametrial structures is entirely independent of how the local cervical lesion is treated, whether by radium or x-rays administered with an intravaginal cone.

ADVANTAGES OF METHOD

Intravaginal ionization measurements would indicate that considerably greater quantities of radiation can be delivered into the pelvis with the aid of pneumoperitoneum. The removal of the intestines from the pelvis permits greater initial dosage, not only on account of the removal of the sensitive intestinal mucosa but also because of the removal of the obstruction caused by the intestines themselves. Likewise, with the intestinal structures high in the abdomen, the lower parts of the abdomen are more readily compressible; compression alone materially increases depth dose, by decreasing thickness. Ischemia of the skin from pressure also decreases the degree of reaction, an effect which we have noted over these parts.

The removal of the underlying soft-tissue structures also removes material which is responsible for part of the back-scattering effect on the skin, thus permitting a somewhat greater initial skin dosage which in turn, having almost uninterrupted access to the parametrium, should produce a somewhat greater dose. Also multiple x-ray beams directed in this way produce in effect a certain amount of cross-firing which should materially increase the parametrial dosage.

RESULTS

Too few patients have been treated in this way and too short a time has elapsed for any estimate of its value. After all, the use of pneumoperitoneum and Trendelenburg's position during x-ray treatment of pelvic cancer is concerned principally with the parametrial areas and has nothing to do with the method by which the primary growth is treated, whether by radium or intravaginal x-ray irradiation. The patients upon whom this method was first used were those who refused use of radium; for that reason we felt obliged to use every method possible to treat their primary lesions as well, and intravaginal radiation with a cone was employed. While intravaginal radiation has great potential possibilities, there is no reason why the pneumoperitoneum method should not be used in association with radium treatment of the primary growth. It is even conceivable, although we have not yet tried it, that this might become a feasible office procedure, since patients with pneumoperitoneum after twenty-four hours often are ambulatory without material discomfort.

606 Missouri Theatre Bldg.
St. Louis, Mo.

BIBLIOGRAPHY

1. DENIS, W., AND MARTIN, C. L.: Toxic Effects Produced by Radiation. Am. J. M. Sc. **160:** 555-567, 1920.

2. WARREN, S. L., AND WHIPPLE, G. H.: Roentgen-Ray Intoxication. J. Exper. Med. **35:** 187-203, 203-211, 1922.

3. DRAGSTEDT, L. R., MOOREHEAD, J. J., AND BURCKY, F. W.: Intestinal Obstruction. J. Exper. Med. **25:** 421-439, 1917.

4. MARTIN, C. L., AND ROGERS, F. T.: Intestinal Reaction to Erythema Dose. Am. J. Roentgenol. **10:** 11-19, 1923.

5. FISCHER, B.: Über Bestrahlungsnekrosen des Darmes. Strahlentherapie **13:** 333–358, 1922.

6. ARNESON, A. N.: Distribution of Radiation within the Average Female Pelvis for Different Methods of Applying Radium to the Cervix. Radiology **27:** 1–20, 1936.

7. PACK, G. T., AND LIVINGSTON, E. M. (Editors): Treatment of Cancer and Allied Diseases. New York, Paul B. Hoeber, Inc., 1940.

8. SANTE, L. R.: Pneumoperitoneum as an Aid in Pelvic Irradiation for Carcinoma of the Cervix. Am. J. Roentgenol. **46:** 689–699, 1941.

9. SANTE, L. R.: A Simplified Pneumoperitoneum Technique. Am. J. Roentgenol. **9:** 618–622, 1922.

10. SANTE, L. R.: Manual of Roentgenological Technique. Ann Arbor, Mich., Edwards Bros., 9th Edition, 1942, pp. 181–186.

11. ARNESON, A. N., AND QUIMBY, E. H.: Distribution of Roentgen Radiation Within the Average Female Pelvis for Different Physical Factors of Irradiation. Radiology **25:** 182–197, 1935.

12. MERRITT, E. A.: Roentgen Therapy of Cancer in the Buccal Cavity and of the Cervix Uteri. Am. J. Roentgenol. **42:** 418–422, 1939.

Intravaginal Roentgen Irradiation of Cancer of the Cervix[1]

W. WALTER WASSON, M.D.

Denver, Col.

THIS PAPER PRESENTS another method for the intravaginal roentgen irradiation of cancer of the cervix.

TECHNIC

Cylinders, as shown in Figure 1, are used to limit the distribution of the rays. These cylinders are made of brass with the thickness of the wall suitable to the voltage used. The diameter of the cylinders varies from 2 to 4 cm.. and the size selected for the individual case is that necessary to fit the vaginal orifice just snugly. A light such as used in the proctoscope (Fig. 2) is fitted to the various cylinders by ring adjusters of appropriate size. These rings and the proctoscopic light, with inflation as used in the ordinary proctoscope, enable the operator to inflate the vagina and to place the cylinder in the desired position in relation to the cervix.

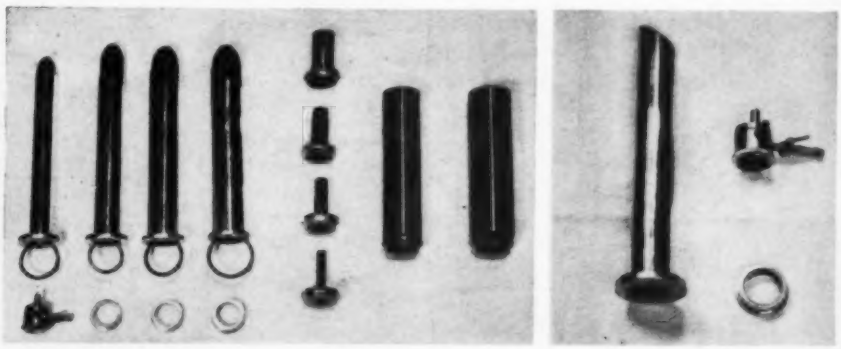


Fig. 1. Assortment of cylinders, obturators, adaptors, and the eye piece used in intra-orificial roentgen irradiation.
Fig. 2. Cylinder, eye piece, and adaptor ring unassembled.

This apparatus, consisting of a cylinder and proctoscopic light, with air inflation (Fig. 3), will be found to be of unusual value in the examination of the vagina and to have a distinct advantage over the customary "bivalve speculum." With the cylinder in the vagina and in proper position, and the rays directed into any desired plane of the pelvis, the light and inflation bulb are removed. The apparatus containing the x-ray tube (Fig. 4) may then be brought into contact with the cylinder and clamped in position. Clamps suitable for holding the cylinder either to the table or to the apparatus containing the x-ray tube may be easily designed for any make of equipment. The table should be clamped in position on the floor and likewise the x-ray tube should be held firmly in position. A periscope (Fig. 4) is desirable for checking the position of the cylinder after the apparatus and table have been clamped in position. This entire procedure will take very little longer than the time required for the insertion of the ordinary vaginal speculum and with no discomfort to the patient. Any desired kilovoltage may be used and any length of time of exposure.

I have found, after three years' experience with this technic, that 200 kv., with the usual factors, is the preferred voltage;

[1] Presented, as part of a Symposium on Carcinoma of the Cervix Uteri, before the Radiological Society of North America, at the Twenty-eighth Annual Meeting, Chicago, Ill., Nov. 30–Dec. 4, 1942.

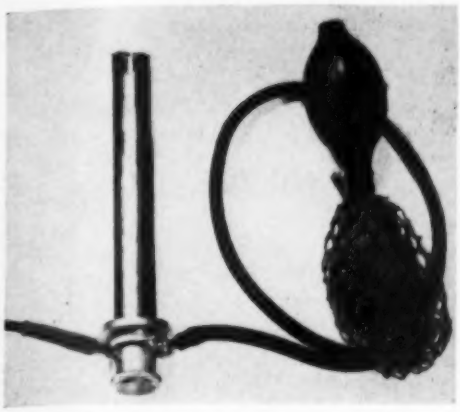


Fig. 3. The cylinder, eye piece, and air compressor, assembled.

age to each area are dependent upon the external radiation that has been or is being given. The cylinders may be angled to direct the rays into the cervix or into the broad ligaments or any portion of the pelvis. An excellent plan which gives a uniform distribution of radiation throughout the pelvis is that shown in Figure 5. Here the first treatment, 1, is given directly into the cervix. Areas 2, 3, 4, and 5, are then treated clockwise as shown in the figure with the cylinder angled to the proper degree to cover the entire pelvis. The intravaginal end of the cylinder should be far enough from the cervix to include the vaginal wall some distance from the visible lesion in

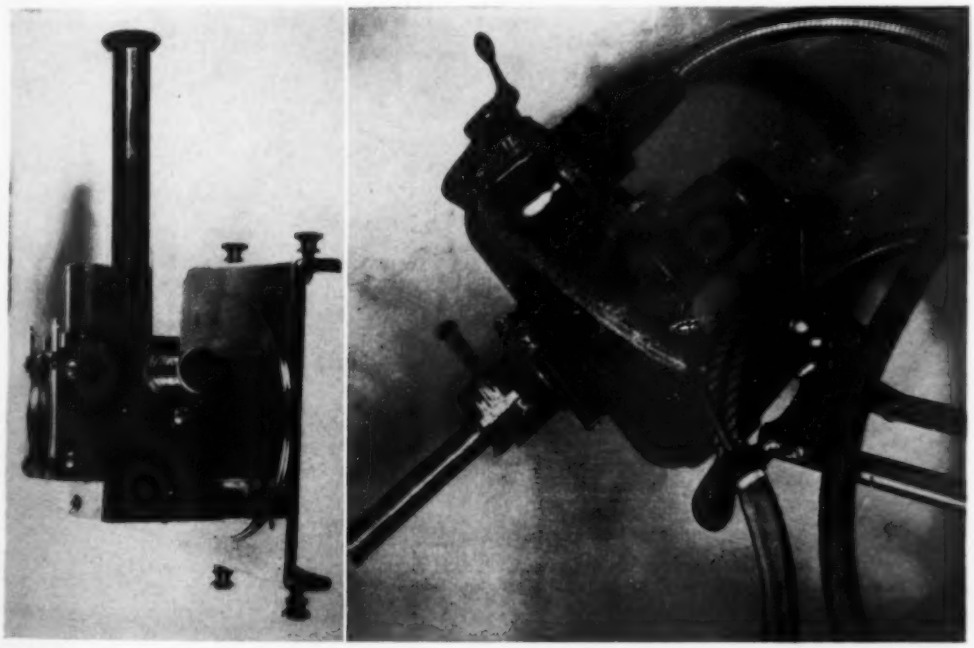


Fig. 4. At the left is the periscope, showing base for attachment to tube head and the receptacle for the cylinder At the right the cylinder and periscope are shown attached to the tube head.

140 kv.-technic may be used in some very superficial conditions. Intravaginal irradiation is always combined with external roentgen irradiation of the pelvis; 250 to 300 r as measured in air are administered to each area at each treatment, and one to two areas are treated daily. The number of areas treated and the dosorder to include in the area of irradiation all possible malignant tissue. It must be remembered that the rays are limited to an area conforming to the diameter of the cylinder. In the application of radium in the cervix there is a wide distribution of rays in all directions, unless these rays are limited by filters.

COMMENT

The therapy of cancer by radiation has not yet reached such a degree of perfection that the radiologist is satisfied with his technic. Each one of us undertaking such a responsibility as the treatment of malignant growth, in any of its forms, is constantly seeking more efficient methods to overcome our high percentage of failures. While the physician has never been able to combat any disease when that disease is encountered in its terminal stage, the percentage of cures of cancer by radiation has not yet reached that degree of perfection whereby only the most severely malignant cases are lost. The effectiveness of x-radiation for the destruction of malignant cells cannot be denied, but to apply these rays successfully for the complete destruction of these cells in the living patient will severely tax the ingenuity of any radiologist. Successful results are dependent upon equipment, the ingenuity and persistence of the radiologist, and the susceptibility of the tumor cells and their accessibility. The technic described makes cancer of the cervix a superficial lesion and enables the radiologist to exhibit a varied program for each individual case.

The advantages of the technic presented are, therefore, those of making cervical cancer a superficial lesion and of affording a method for the uniform distribution of the x-rays to the female pelvis. Greater dosages may be given to strategic points than by any other method, even including radium. When this method is combined with Sante's technic of pneumoperitoneum, even larger dosages may be utilized than I have given. The broad ligaments may especially be selected for attack, leaving the bladder and rectum isolated from the rays. Or again, the floor of the bladder or the anterior rectal wall or an isolated tumor following hysterectomy may receive x-rays by the cross-fire technic from within the vagina. These advantages give the radiologist an opportunity to study his patient and to have at his command another procedure for the treatment of cancer of the cervix besides that of radium and the cus-

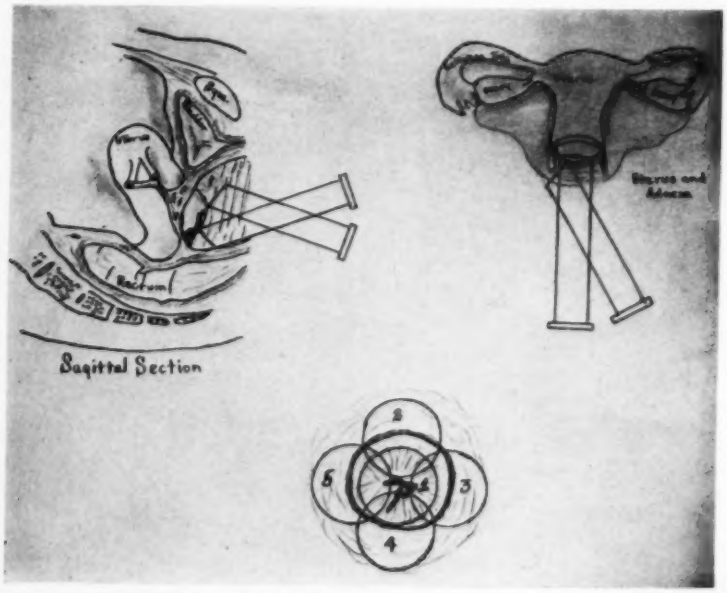


Fig. 5. Diagrammatic sketch showing the relationship of the cylinders to the areas treated and the uterine adnexa. The lower diagram shows the areas treated as they would be seen through a speculum.

tomary external application of roentgen rays. There are those cases where the implantation of radium into the cervix or the uterine cavity will be desirable in addition to both intravaginal and external application of x-rays. In any case the tolerance of the vaginal wall or of the pelvic viscera will determine the maximum dosage which it is possible to give.

The advantages of the technic presented seem to outweigh the disadvantages. The apparatus which has been described offers no handicap either as to cost or as to construction. It is both simple and economical. There is very little discomfort for the patient. The greatest disadvantage is the meticulous nature of the technic. Care must be exercised in the placing of the cones in order to treat the cervix and at the same time distribute the rays uniformly throughout the pelvis. The time involved at each individual application is negligible, but the number of treatments adds to our already lengthy course of irradiation of the pelvis in cancer of the cervix. This is a definite handicap in a busy clinic which may be already too overloaded for the proper care of these patients.

RESULTS

It is the object of this paper to present a technic for the intravaginal x-irradiation of cancer of the cervix rather than to state the results of this technic. After three years of employing this method I would prophesy that the results as to permanent cures will be no better in the early cases than those of radium and external roentgen therapy. There will be, however, less necrosis of the cervix and likewise less infection of the vagina when this technic is employed in the early cases. It is possible to arrive at a uniform distribution of the rays through the pelvis without the necrosis of the cervix following the application of radium. The results in advanced cases should be better than by any of the other methods which have been at the command of the radiologist. In these cases radium may be applied as seems advisable, intravaginal roentgen radiation may be given for still further uniform distribution of the rays through the pelvis, and external application of the roentgen rays may be used to supplement both the radium and the intravaginal x-radiation. The failures after this combined treatment will then more nearly parallel those hopeless cases where the cancer is not only very extensive but also very resistant to any method of radiation therapy. In other words, there will still be those who do not respond to the most uniform distribution of either the gamma or the roentgen rays in optimum dosage.

SUMMARY

1. Another technic is presented for the intravaginal roentgen irradiation of cancer of the cervix.

2. The disadvantages and the advantages of this technic are discussed.

3. Better results after irradiation of the female pelvis in cancer of the cervix are to be expected.

4. The apparatus described has a distinct advantage for the routine examination of the vagina.

304 Republic Bldg.
Denver, Colo.

Further Study of Supervoltage X-Ray Therapy in Carcinoma of the Cervix[1]

HERBERT E. SCHMITZ, M.D., F.A.C.S.

Chicago, Ill.

TEN YEARS HAVE elapsed since the first patient suffering from carcinoma of the cervix was treated with roentgen rays in the region of 800 kv. maximum at the Mercy Hospital Institute of Radiation Therapy. Numerous publications (6, 7, 8, 9, 11) by our staff have appeared, stating our observations of the effect of such vol-

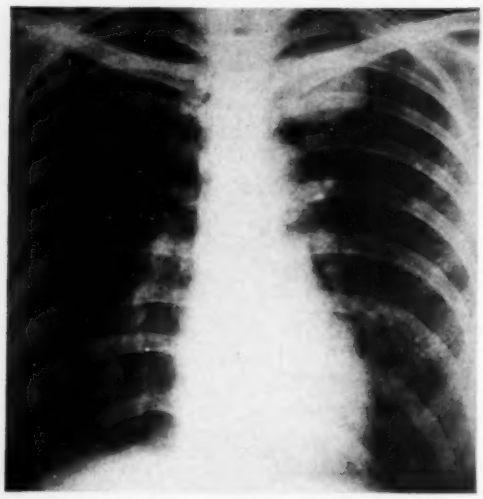


Fig. 1. Case I: Roentgenogram of chest showing mass in upper left lung.

tages on the patient, the blood stream, and the tumor cells themselves. In 1938, before this Society, the late Henry Schmitz (10), founder of our Institute, participating in a symposium on carcinoma of the cervix, reported the action of 800 kv. roentgen rays on the tumor and on the carcinoma cells with known radiation doses, giving the survival rates after three, four, and five years. In the present study the five-year end-results will be brought up to date, and two cases with survival for four and six years, respectively, and the ultimate development of unusual metastatic lesions will be reported in detail. These cases have been considered of sufficient importance to present at this time because of the infrequency of such metastases and the difficulty encountered in arriving at a correct diagnosis.

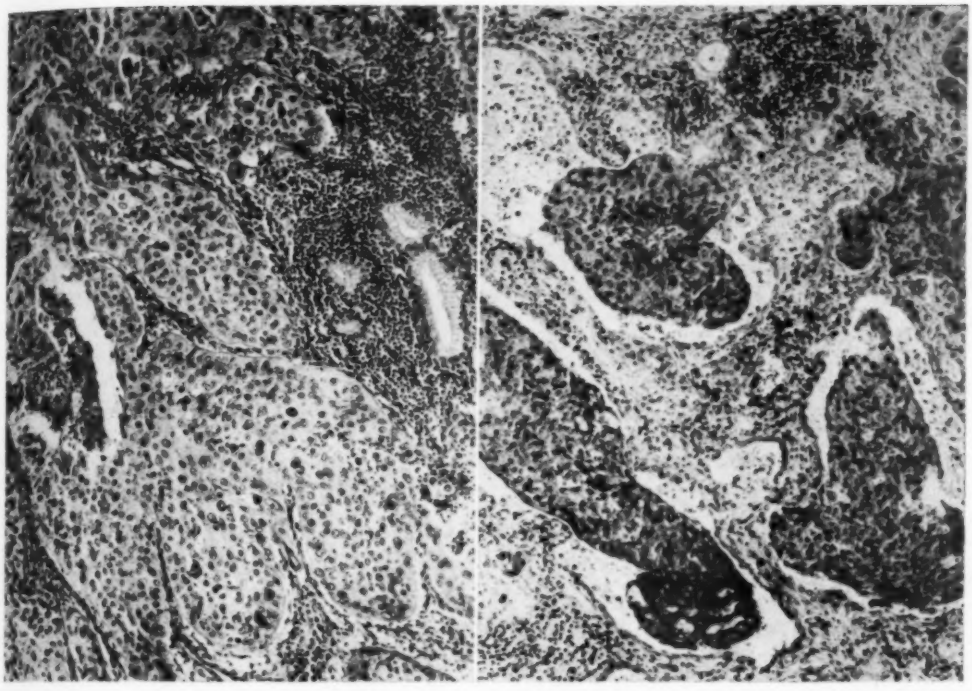
The clinical grouping of Schmitz has been used to divide the cases for study and evaluation of the therapy. The factors of x-ray production, the distribution of radiation intensities within the tissues traversed by the roentgen-ray beam, and the method of treatment have been reported in earlier communications and will not be discussed here.

CASE REPORTS

CASE I: Mrs. G. R., a 32-year-old woman (gravida II; para 0), was first treated in August 1935 for a carcinoma of the uterine cervix of clinical group II. The pathological diagnosis was primary infiltrating plexiform epidermoid carcinoma of the cervix, Grade III R.S. A complete course of x-ray and radium therapy according to our published technic was administered. The cervical lesion healed following this treatment, and the patient remained free of symptoms until December 1941, when she was readmitted to the hospital complaining of a cough of several months' duration, accompanied by a progressive weight loss. Physical examination at this time revealed a small area of dullness in the left upper lung. Breath sounds were increased over this area. Pelvic examination showed the vaginal walls to be smooth and pliable. The cervix was infantile in size, smooth, and completely epithelialized. The corpus was in normal position, small, and freely movable. The adnexa were negative on palpation, and the parametrial tissues were free. The diagnosis was healed carcinoma of the cervix and possible pulmonary tuberculosis.

Roentgenograms at this time revealed an encapsulated mass in the upper left lung. Sputum examinations were negative for tubercle bacilli, but the

[1] From the Department of Obstetrics and Gynecology, Loyola University School of Medicine and the Mercy Hospital Institute of Radiation Therapy. Presented, as part of a Symposium on Carcinoma of the Cervix Uteri, before the Radiological Society of North America, at the Twenty-eighth Annual Meeting, Chicago, Ill., Nov. 30–Dec. 4, 1942.



Figs. 2 and 3. Case I: Fig. 2 (left) is from the original biopsy specimen from the cervix (Sept. 6, 1935), showing large islands of infiltrating plexiform squamous-cell carcinoma (Grade III), chronic inflammation, and several small pale endocervical glands (×90).

Fig. 3 (right) is a section of the lung obtained at autopsy (Jan. 31, 1942), showing metastatic squamous-cell carcinoma, tumor within the alveoli, and chronic pneumonitis (×90).

temperature showed slight daily elevations. The diagnosis was then changed to benign tumor of the lung. The patient rapidly lost strength, and on Jan. 1, 1942, a mass, firm and moderately tender, could be palpated in the epigastrium. Death occurred on Jan. 31, 1942. Autopsy revealed metastatic carcinoma of the left upper lobe of the lung, healed carcinoma of the cervix, and metastatic carcinoma of the liver.

CASE II: Mrs. A. R., a 66-year-old woman (gravida III; para III), was first seen in June 1938, at which time a carcinoma of the cervix of clinical group II was found. According to the microscopic report this was a rapidly growing, poorly differentiated epidermoid carcinoma, growing mainly in spindle form, Grades II–III. This was treated with radium and x-ray according to our technic. In May 1939 a papillary growth, a centimeter in diameter, was discovered on the anterior vaginal wall, to the left of the urethra and 2 cm. from the introitus. Biopsy showed this to be a squamous-cell carcinoma of moderately rapid growth, Grade II. Fifty (50) mg. of radium element in a 1.5-mm. brass capsule were inserted in a bakelite phantom, and this was placed into the vagina for twenty-four hours. Following this the vaginal lesion healed and the vaginal walls became agglutinated. The patient remained free of symptoms until October 1941, when she returned, complaining of pain and a persistent burning sensation over the region of the left scapula, precordial distress, and pain in the left flank. Chest examination revealed dullness over the upper third, and increased voice and breath sounds. Roentgenograms demonstrated a new growth involving the lung in this area. Vaginal examination showed the vaginal walls to be firmly agglutinated. The recto-vaginal septum was smooth and pliable. The cervix could be palpated as a smooth nub. The uterus was freely movable, the adnexa were negative on palpation, and the parametrial tissues were free. The diagnosis at this time was arrested carcinoma of the cervix and vagina and metastatic carcinoma of the left lung.

The patient failed rapidly; an epigastric mass and left-sided hemiplegia developed. Death occurred on Nov. 13, 1942.

The diagnosis was arrested carcinoma of the cervix and vagina, metastatic carcinoma of the liver, lung, and brain.

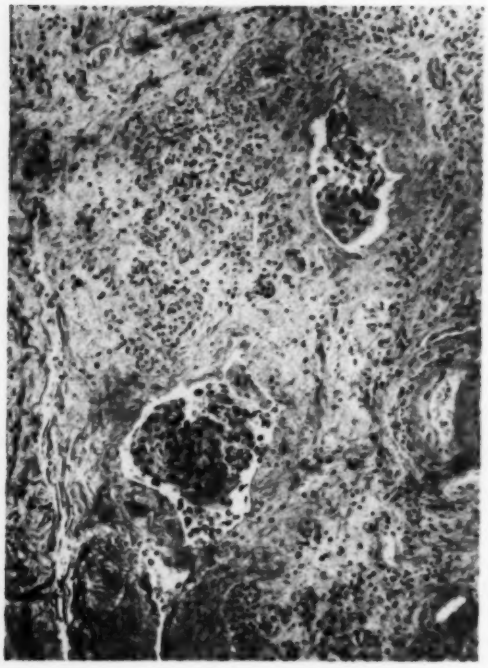


Fig. 4. Case I: Autopsy specimen (Jan. 31, 1942) from uterus. The presence of tumor cells lying in endothelial-lined channels (small veins with few red cells not too well shown at this power) indicates hematogenous dissemination. Radiation changes in vessels; myometrium (×90).

COMMENT ON CASES

In previous reports describing the effect of radium and 800 kv. roentgen rays on the carcinoma cells, it was pointed out that small clumps of altered tumor cells remained incarcerated in an abundant stroma. Many cells persisted only as basophilic smudges. It is evident that the finding of completely degenerated carcinoma cells, albeit a complete absence of tumor cells, should not be interpreted as a cure but as an instance of the profound effect of the 800-kv. rays on a deeply seated cervical cancer. The two cases presented here are examples of how these altered tumor cells may at a much later date regain activity and cause distant lesions not commonly seen in association with cancer of the cervix. Mitchell and Angrist (5) state that there are two possible routes which tumor emboli may take to reach the brain from the pelvis. One is the pulmonary bed, the other the vertebral system of veins. In the cases recorded here emboli undoubtedly reached the lungs through the venous system, where they had remained dormant for years, and in the second case finally extended to the brain.

In Case I the lung lesion (Fig. 1) had none of the characteristics of a metastatic lung tumor, and surgical exploration was contemplated. Appearance of the epigastric mass forestalled this procedure. Comparison of the original biopsy specimen (Fig. 2) from the cervix shows it to be similar to the tissue (Fig. 3) taken at autopsy from the mass in the lung. Gross examination of all the tissues in the pelvis failed to reveal any carcinoma remaining in these organs or tissues. Figure 4, however, shows definite emboli of tumor cells remaining six years after treatment.

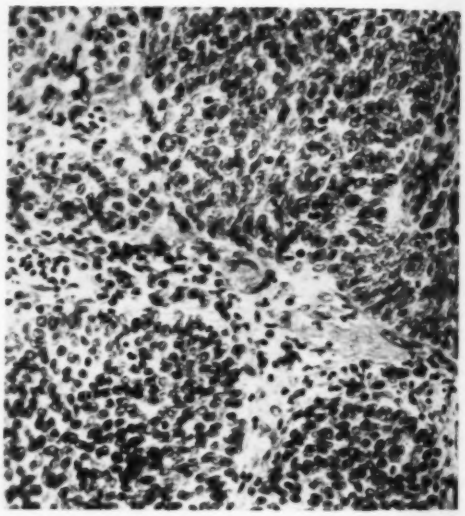


Fig. 5. Case II: Biopsy specimen from cervix (June 9, 1938). Rapidly growing poorly differentiated epidermoid carcinoma growing mainly in spindle cell form, (Grade II–III) (×210).

Case II is included here because of the similar course of the disease. Figure 5 shows the primary tumor, and Figure 6 shows the lung metastases. At no time was it possible to demonstrate a local

recurrence in this case after the first vaginal implantation had been destroyed. Although there was not an autopsy to substantiate the diagnosis of pulmonary and cerebral metastases without apparent pelvic activity, we feel quite sure clinically that this was the case.

Finding of such metastases in cases of carcinoma of the cervix makes necessary a change in our teaching regarding these tumors. Cervical carcinomas were always thought to remain localized within the pelvis, extending only through the lymphatic spans in the connective tissue. This is, of course, the chief method of advance. Auster and Sala (2), studying 124 autopsied cases of cervical cancer, found examples in which the nodes nearest to the cervix were spared while metastases were set up in more distant nodes, probably by tumor embolism. They conclude that blood-borne metastases are not rare nowadays. They write: "We believe that they occur very late, and their more frequent occurrence is to be explained only by the fact that more patients are enabled to live long enough to get them." Stone and Robinson (12), having carefully reviewed the literature, stressed the importance of this fact in planning the number and size of fields through which x-ray therapy is to be given. They agree with Arneson and Quimby (1) that six fields produce the best internal distribution of the radiation and give the greatest assurance that all pelvic nodes are included in the radiation beam. No mention is made of the possibility of blood-borne metastases.

As our improved technics of treating carcinoma of the cervix result in more patients surviving for longer periods of time, these distant metastases through the blood stream to the bone, liver, lungs, and brain will become more common.

RESULTS OF TREATMENT

Two hundred thirty-four patients with carcinoma of the uterus were admitted to the Gynecologic Service of the Mercy Hospital Institute from May 1933 to Jan. 1 1938. Those having had treatment prior to admission were excluded from this study as our results were consistently bad in cases which had been partially or improperly treated. Higher-voltage therapy has nothing additional to offer these patients. After elimination of the corpus cancers, which have recently been reported, there remain 72 cases of primary, previously untreated carcinomas of the cervix.

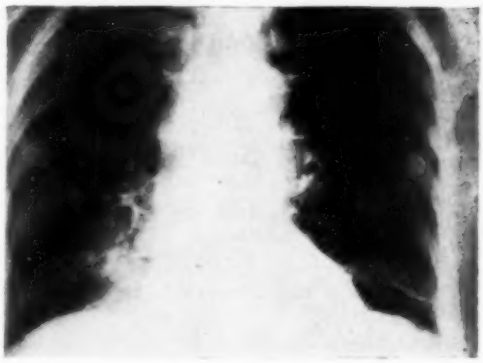


Fig. 6. Case II: Chest roentgenogram showing lung metastases.

Table I shows the cases grouped according to their clinical extent, giving the number of survivals in each group and the percentage of survivals per group and for all groups.

TABLE I: RESULTS OF TREATMENT

Clinical group . . .	I	II	III	IV	Total
Number of cases..	3	16	32	21	72
Well 5 years.....	3	8	14	2	27
Percentage well 5 years.....	100%	50%	43%	9.5%	37.5%

The cases here presented are additional evidence that the two main facts influencing our end-results are: (1) that in clinical Groups I and II carcinoma of the cervix can be arrested in 75 per cent of cases, but (2) the greatest number of cases fall in clinical groups III and IV, where only 26 per cent can be salvaged. The total five-year salvage rate is lower than the 41.6 per cent previously reported, but it is about the same as that given by Kamperman (4) for a group of similarly treated

cases. This group embodies a sufficient number of cases so that we believe future additions will cause little change in this figure.

25 East Washington St.
Chicago, Ill.

REFERENCES

1. ARNESON, A. N., AND QUIMBY, E. H.: Radiology **25:** 182–197, 1935.
2. AUSTER, L. S., AND SALA, A. M.: Surg., Gynec. & Obst. **71:** 231–239, 1940.
3. BARANAY, E., AND SALA, A. M.: Am. J. Roentgenol. **44:** 579–585, 1940.
4. KAMPERMAN, G.: Surg., Gynec. & Obst. **72:** 384–390, 1941.
5. MITCHELL, N., AND ANGRIST, A.: Am. J. Clin. Path. **12:** 232–238, 1942.
6. SCHMITZ, H.: Radiology **25:** 341–348, 1935.
7. SCHMITZ, H.: Radiology **26:** 331–334, 1936.
8. SCHMITZ, H.: Am. J. Obst. & Gynec. **33:** 74–79, 1937.
9. SCHMITZ, H., SCHMITZ, H. E., AND SHEEHAN, J. F.: Am. J. Obst. & Gynec. **35:** 405–415, 1938.
10. SCHMITZ, H.: Radiology **34:** 34–37, 1940.
11. SCHMITZ, H. E., AND SHEEHAN, J. F.: Am. J. Roentgenol. **45:** 229–234, 1941.
12. STONE, R. S., AND ROBINSON, J. M.: Radiology **36:** 521–533, 1941.

Tissue Dosage in the Control of Carcinoma of the Cervix[1]

MANUEL GARCIA, M.D.

New Orleans, La.

At the Charity Hospital of Louisiana, in New Orleans, responsibility for the treatment of carcinoma of the cervix was assigned to the Department of Radiology in April 1938. Only three years have elapsed, therefore, since the first group of cases was treated, but this interval of time is probably sufficient to reveal errors in the management of the disease and to provide suggestions for enhancing the effectiveness of the plan of treatment followed. Our interest was directed to the dosage range attained in the pelvis with the method of irradiation employed, and the present report attempts to correlate the doses delivered and the end-results observed.

Studies on this subject have appeared in the literature for more than a decade. Without intending to be exhaustive one can mention those of Healy (1), Arneson (2), and Lucas (3), who have shown the distribution of radiation in the pelvis for the more important radium technics. These writers have indicated the tissue doses in threshold erythemas, whereas Murdoch (4), pursuing similar investigations, expressed them in absolute units, that is, in ergs per cubic centimeter, basing his values partly on calorimetric determinations. Mayneord has pointed out the inaccuracies of this method and has given the complete three-dimensional distribution of radiation in the pelvis for the Marie Curie Hospital technic (5), as well as methods for calculating the total quantity of energy absorbed during treatment (6). Mayneord, Sandler (7), and others have expressed the gamma ray doses in roentgens. The information now available on the standard treatment technic can thus be considered fairly complete. In practice, however, departures from a standard plan of treatment are frequent, since no set technic, ably designed though it be, can be expected to cope with all the variations exhibited by the disease. Indeed, flexibility is a decided advantage. Improvement in the results of radiation therapy, therefore, must come from evaluation of the actual tissue dosage attained in patients under treatment. This has been done in the studies reported by Frazell (9), Tod (10), and Reinhard and his coworkers (11). Our intention is simply to provide additional data along the same lines.

The material for this analysis comprises 191 primary cases of carcinoma of the cervix treated at Charity Hospital from April 1, 1938, to August 31, 1939. The absolute three-year survival rate for the group was 37.7 per cent. For the purposes of this study 8 cases have been eliminated, either because they received no treatment at all or because the data recorded were insufficient for calculation. Two patients who died from complications of radium therapy have also been excluded. Among the 72 survivors, 5 had recurrences before the end of the third year and are classed as radiation failures.

A combination of x-ray and radium therapy was employed whenever possible. Treatment usually began with external x-ray therapy in accordance with the technic described by Arneson and Quimby (12). The dose amounted to 1,600 to 2,000 r in air through each of six pelvic ports (10 × 15 cm. in dimensions), with the following factors: 200 kv., 0.5 mm. of Cu and 1 mm. Al filtration, H.V.L. 0.9 mm. Cu, 20 ma., and 50 cm. distance. In addition, 65 of the patients had pervaginal x-ray therapy according to the method

[1] From the Department of Radiology of the Charity Hospital of Louisiana, and of the Tulane University of Louisiana School of Medicine. Presented, as part of a Symposium on Carcinoma of the Cervix Uteri, before the Radiological Society of North America, at the Twenty-eighth Annual Meeting, Chicago, Ill., Nov. 30–Dec. 4, 1942.

described by Cooper (13), with 90 kv., no filter (H.V.L. 1 mm. Al), 4 ma., 35 cm. distance and a cone 4 cm. in diameter. The dose by this route ranged between 1,200 and 7,200 r in air. Radium therapy was administered by a modification of the technic of Regaud and Lacassagne (14). With 1.5 mm. Pt filtration, from 5,000 to 8,000 mg. hr. of radium were given in a period of four to eight days, about half in the cervical canal and half in the vaginal fornices. Four patients received radium therapy only, while 42 had x-ray therapy only. The total duration of treatment varied from three to one hundred and thirty-seven days, including the time elapsing between x-ray and radium therapy, or between radium treatments when the latter had to be interrupted on account of infection.

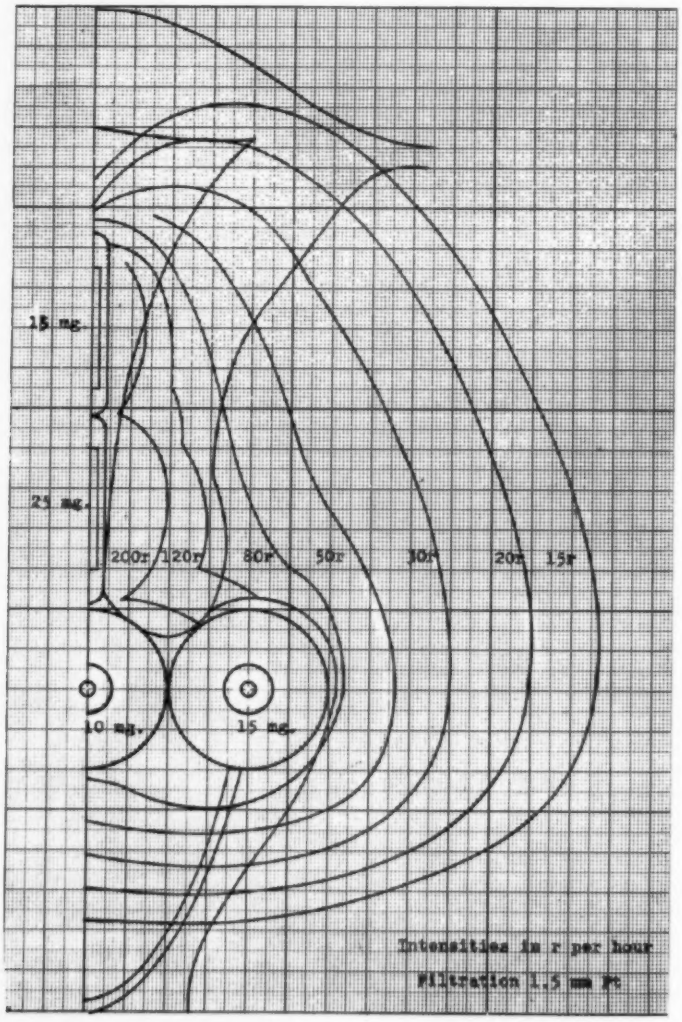


Fig. 1. Isodose curves in the coronal plane of the pelvis for a frequently employed distribution of radium. Gamma ray intensities are indicated in r_γ per hour.

The x-ray doses delivered within the pelvis have been calculated from the depth dose data given by Quimby (15) and the gamma ray doses from Sievert's formula for tubular sources (16). The r-conversion factor in the formula, however, was not derived from the value of 7.55 given by Sievert but from that given by White, Marinelli and Failla (17), *i.e.*, 8.47 r/mg. hr. under standard conditions. Figure 1 gives the isodose curves for a frequently used distribution of the radium. Gamma ray intensities are indicated in r_γ per hour.

In attempting to evaluate the significance of the computed doses, three problems arise: specification of the dose in a common unit for all the qualities of radiation employed so that the amounts can be added; selection of points in the pelvis where the dose has a bearing on the end-results; determination of the effect produced on the magnitude of the dose by variation in the duration of treatment.

Both x-ray and gamma ray doses can now be expressed in roentgens, but even when specified in this manner such doses cannot be added (Quimby, 18), since the biologic effect is not a constant function of the amount of radiation when the average or effective wavelength is changed. The correct procedure has been indicated by Failla (19); this consists in conversion of the computed doses to the equivalent amounts in one of the qualities employed. Accordingly it was decided to convert gamma ray and low-voltage x-ray doses to the equivalent amounts of 200 kv. x-rays. To accomplish this, the conversion factors should be obtained properly from the ratios of the lethal doses for carcinoma of the cervix for the three qualities specified. Unfortunately such information is not available and approximate values for the conversion factors must be obtained indirectly. The doses required to produce a threshold erythema in human skin are undoubtedly most suitable for this purpose, as they have the advantage of long clinical application. But experience in the treatment of carcinoma of the skin (20) and of the bladder (21) suggests that the conversion factor for low-voltage x-rays derived in this manner is too high. Because of the variation in the time factor, however, the data provided by clinical studies cannot be used to gain a more correct figure. For this reason experimental investigations free from this objection have to be consulted; relevant information from such sources appears in Table I. Only a few values are given, since a comprehensive review of the subject is obviously beyond the scope of this paper. Consideration of the ratios given leads us to believe that acceptable values for the conversion factors are 0.6 for gamma rays (cf. Walker, 25) and 1.5 for low-voltage x-rays. These agree with clinical impressions and have been adopted for the present study. It is regrettable that the intervention of artificial selection could not be completely excluded.

TABLE I: RATIO OF THE DOSE OF 200 KV. X-RAYS TO BIOLOGICALLY EQUIVALENT DOSES IN OTHER QUALITIES

Author	Reaction Tested	Ratio for Gamma Rays	Ratio for Soft X-Rays
Quimby (15)	Threshold erythema, human skin	0.68	2.5
Lasnitzki and Lea (22)	Inhibition of mitosis in tissue culture	0.49	1.1
Lea (23)	Delayed lethal action in chick embryos	0.6	1.1
Mottram and Gray (24)	Erythema, desquamation, tail skin of mice	0.77	...
	Exudation, epilation, tail skin of mice	0.62	...
	Conversion factors chosen	0.6	1.5

Figure 2 shows the dosage range in the coronal plane for the combined treatment with 8,000 mg. hr. of radium, distributed as in Figure 1, and x-ray therapy amounting to 1,600 r to each of six ports, as previously specified, in a pelvis of average dimensions; in our cases these were 18 × 30 cm., measured with compression. The quantities of radiation bear the subscript q to indicate that they have been corrected for quality.

In estimating the effectiveness of radiation in controlling carcinoma of the cervix, the minimum tumor dose should logically be the quantity calculated. The actual extent of the tumor is hard to determine, but Frazell has suggested that certain arbitrary limits be set for each of the stages and he has demonstrated that, as one increases the dose delivered to the points he defined, the end-results improve. Another approach to the problem has been made by Tod and Meredith (26), who determine the tolerance dose received in the pelvis. They believe that a conical area surrounding the cervix, which they have called the paracervical triangle, is the limiting factor in the amount of radiation that can be delivered. The dose is assessed at a point 2 cm. lateral to the mid-line and 2 cm. above the vaginal fornix. Subsequently Tod (10) and Reinhard *et al.* (11) have correlated the end-results of treatment and the amount of radiation reaching this point (P, in Fig. 2), which in reality indicates the dose delivered to a relatively large zone, as can be seen from the isodose dia-

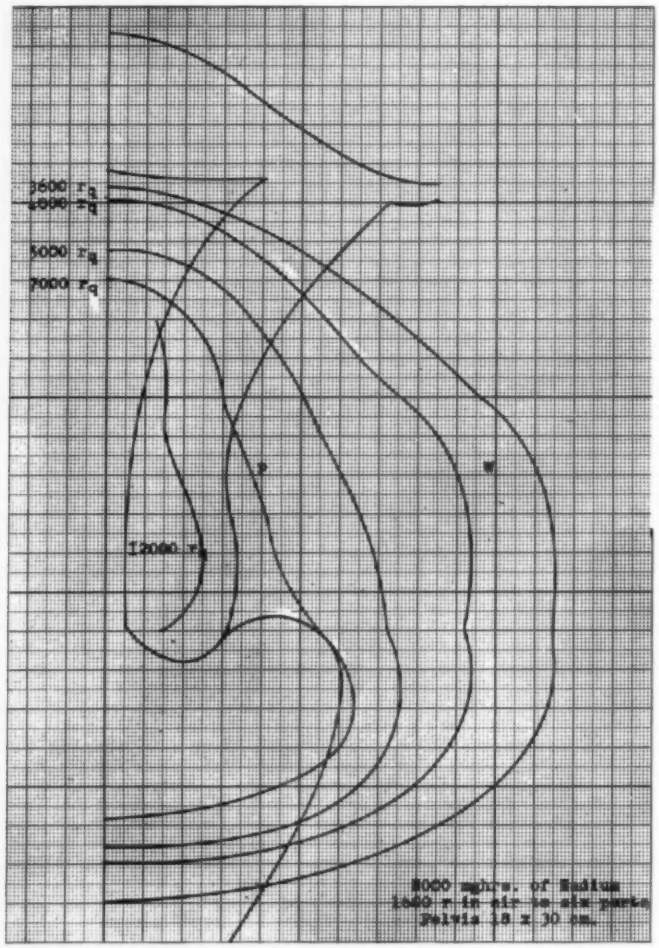


Fig. 2. Isodose curves in the coronal plane of the pelvis for the combined treatment with radium and x-ray. Paracervical dose calculated at point *P*, pelvic wall doses at point *W*.

gram, and probably represents the minimum tumor dose for stages I and II. The recovery rates for doses calculated in this manner are given in Table II for all our cases. In the same table the recovery rates for stages I and II are contrasted with those for stage III, using for the former the paracervical doses and for the latter the doses at the pelvic wall (point W). The concentration of cases lies in different segments of the range, so the subgroups are probably too small to yield significant results. The recovery rates show a rough parallelism, but it is not adequate to establish a consistent relation between the quantity of radiation presumably delivered to the periphery of the tumor and the proportion of cases controlled.

The doses tabulated are open to the serious objection that variation in the time factor has been ignored. For this reason it becomes necessary to determine how the magnitude of the dose required to control the neoplasm is affected by the duration of treatment. It is obviously impossible to ascertain this with precision from the information at our disposal, but some useful facts may be elicited.

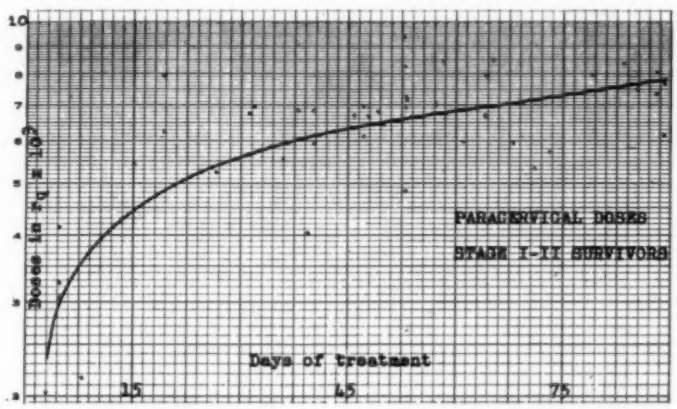


Fig. 3. Curves showing the relation of the magnitude of the dose at the paracervical area and the duration of treatment in 44 stage I – II survivors. Dots indicate doses in individual cases.

TABLE II: PARACERVICAL DOSES

	No. of Cases	Survivors	Rates
ALL CASES			
Less than 2,000 r_q	21	0	0%
2,000–4,000 r_q	36	5	14%
4,000–6,000 r_q	42	14	33%
6,000–8,000 r_q	56	35	62%
8,000–10,000 r_q	26	13	50%
STAGES I AND II			
Less than 2,000 r_q	5	0	0%
2,000–4,000 r_q	9	5	55%
4,000–6,000 r_q	18	9	50%
6,000–8,000 r_q	29	22	76%
Over 8,000 r_q	13	8	61%
STAGE III: DOSES AT THE PELVIC WALL			
Less than 2,000 r_q	13	1	7%
2,000–4,000 r_q	46	16	35%
4,000–5,000 r_q	13	6	46%

The paracervical doses in 44 stage I and II survivors ranged between 2,010 and 8,490 r_q, and the duration of treatment between three and eighty-nine days. The values are plotted in Figure 3. It can be seen that, as the period of treatment becomes longer, the calculated doses tend to be higher, which, of course, is in accord with well established clinical observations, though in carcinoma of the cervix this is sometimes obscured, as for instance in a comparison of the Paris and the Swedish radium technics. The group of cases shown, however, is small, the plotted values are scattered, and doubt may arise as to whether the suggested relation is

TABLE III: PARACERVICAL DOSES, IN PERCENTAGE OF VALUES FROM THE CURVE

	No. of Cases	Survivors	Survival Rates
ALL CASES			
Less than 60%	54	0	0%
60–100%	60	28	46%
100–160%	67	39	58%
STAGES I AND II			
Less than 60%	11	0	0%
60–100%	27	17	63%
100–160%	36	27	75%
STAGE III			
Less than 60%	21	0	0%
60–100%	25	11	44%
100–160%	26	12	46%
STAGE IV			
Less than 60%	22	0	...
60–100%	8	0	...
100–160%	5	0	...

actual or apparent. The correlation coefficient of dose and time was therefore calculated, and it was found to have an unadjusted value of +0.635, which, when tested for significance by t-transformation, gives a deviation of 6.89, clearly indicating that the relation suggested is real; the probabilities that chance alone could account for it are negligibly small even for a sample of this size. An independent check on this question is provided by analysis of the data furnished by Tod. She has 101 stage I and II survivors showing no high dose effects; though exact correction for quality for the paracervical doses recorded cannot be done, sufficient information is given to arrive at fairly satisfactory approximations. The correlation coefficient for the corrected doses was found to be +0.788. When the two values for the coefficient are converted to the statistical function Z, their difference (0.31589) is less than twice the standard error (0.186). It follows that the two values are not significantly different, and if no gross errors were committed in our interpretation of the data, it may be taken as established then that longer periods of treatment are associated with larger doses in patients successfully treated for carcinoma of the cervix. While this cannot be offered as proof that the increment is essential for the control of the neoplasm, evidence is no longer needed to show that in the production of any biologic effect the quantity of radiation required becomes greater as the period of treatment is prolonged. Consequently it seems justifiable to place the same interpretation on the upward trend observed in the dosage, *i.e.*, that it is an indication of the increase needed to compensate for the loss in biologic effectiveness.

Some idea of the relation of the magnitude of the dose and the duration of treatment may be obtained from the observations plotted by the method of least squares. For this purpose the following equation was chosen empirically:

$$y = a + b\sqrt{x} + c \log x,$$

where y is the dose in r_q, x the number of days of treatment, and a, b, and c constants, the respective values for which were found to be 808.8, 298, and 2,145. The corresponding curve is shown in Figure 3. Naturally the estimates of y are subject to a very large error (± 919.7 r_q), and comparison with the average doses for different periods of treatment in the Tod series gives a value of ± 762.1 r_q for the root mean square of the discrepancies with the curve. With data of this type, better agreement could hardly be expected at present, except in isolated instances, as in the case of the paracervical dose given by Mayneord and Honeybourne for the Marie Curie Hospital technic; the dose contour diagram indicates that this is approximately 120 r_γ per hour; the complete treatment therefore delivers 7,920 r_γ in twenty-two days; this is equivalent to 4,760 r_q and represents 93 per cent of the corresponding dose derived from the equation. Despite the apparent conformity, literal interpretation of the curve as a guide to the optimum doses for different periods of treatment is entirely unwarranted. The discontinuous nature and irregularity of the treatments were not taken into account. But lacking any concept of the true variation of the dose with respect to time, a rough approximation of this sort

may be considered permissible till more reliable information becomes available. Undoubtedly, as more data accumulate, the values for the constants will need to be revised or perhaps a more suitable function substituted.

Assuming provisionally that the curve presented provides a satisfactory line of reference, then it becomes of interest to determine what correlation can be established with the recovery rates. We find that no patient survived when the quantity of radiation delivered was less than 60 per cent of the value given by the curve for the same number of days of treatment, and that the group receiving 100–160 per cent gave somewhat better recovery rates than the one receiving 60–100 per cent of the corresponding doses indicated by the curve. This is shown in Table III. The better rates for the largest doses are not statistically significant, even in the stage I and II subgroups. It can be demonstrated by the Chi square test that the findings are consistent with the supposition that, once the minimum effective dose is exceeded, the number of survivors in each subgroup is proportional to the total number in it, the proportionality factor being dependent on the stage of the disease and not on the dose administered. Apparently this is not an adventitious circumstance; it has been pointed out already by Reinhard, Goltz and Schreiner, who with more abundant material have been able to study narrower dosage bands. This would have detected any intermediate range yielding optimum results, which could have been obscured by the coarser grouping we employed. Their patients were treated in four days and received between 4,000 and 8,000 "r," nearly all gamma radiation; this is approximately equivalent to 85 to 178 per cent of the value from the curve. The five-year survival rates were almost identical for the various segments of the range, averaging 76 per cent in 102 stage I and II cases and 57 per cent in 125 stage III cases treated by "primary irradiation." Subject to the correctness of the initial assumption made, the findings in the two series thus appear mutually consistent despite the difference in the time factor.

The information reviewed leads to the conclusion that the doses tolerated in the paracervical region are far in excess of the quantities required to obtain the maximum beneficial effects with the radiation sources employed. It is very doubtful that the results of treatment in stages I and II can be materially improved. For these cases there seems to be needed only a better definition of the minimum effective dosage levels, so that the doses as a whole can be reduced with safety. Possibly the reduction of the dose in the center of the pelvis in stage III cases would also be advantageous, tending to enhance the tolerance to the greater quantities of radiation that may now be delivered in the region of the pelvic wall with supervoltage equipment; this may yield a greater proportion of survivors. For the present it can be said that it seems possible to deliver doses of radiation which are well tolerated and result in recovery in about three-fourths of stage I and II cases and in nearly half of stage III cases, recovery in this instance meaning clinical control of the disease for three years.

SUMMARY

An analysis of the tissue doses delivered in 181 cases of carcinoma of the cervix treated at Charity Hospital (New Orleans) is presented. The results are assessed at the end of three years. The corrections for quality and for the time factor are discussed and the doses attained are tabulated.

Charity Hospital of Louisiana
New Orleans, La.

BIBLIOGRAPHY

1. HEALY, W. P.: Treatment of Carcinoma of the Cervix Uteri. Ann. Surg. **93:** 451–459, January 1931.
2. ARNESON, A. N.: Distribution of Radiation within the Average Female Pelvis for Different Methods of Applying Radium to Cervix. Radiology **27:** 1–20, July 1936.
3. LUCAS, C. DE F.: Calculation of Dosage in the Radium Treatment of Carcinoma of the Cervix. Am. J. Roentgenol. **36:** 477–489, October 1936.
4. MURDOCH, J., SIMON, S., AND STAHEL, E.: Contribution à l'étude de la dosimétrie en curiethérapie. Acta radiol. **11:** 350–397, 1930.

5. MAYNEORD, W. V., AND HONEYBURNE, J.: Physical Study of Intracavitary Radium Therapy. Am. J. Roentgenol. **45:** 235–249, February 1941.
6. MAYNEORD, W. V.: Energy Absorption. Brit. J. Radiol. **13:** 235–247, July 1940.
7. SANDLER, B.: Investigation into Dosage Delivered by Certain Techniques in Radiation Therapy of Carcinoma Cervix. Brit. J. Radiol. **11:** 623–636, September 1938. Radium Distribution Factor in Carcinoma Cervix Therapy with Comparison of Techniques. Ibid. **14:** 284–293, September 1941.
8. WALKER, J. Z.: Principles of Radiation Treatment of Carcinoma Cervicis Uteri. Edinburgh M. J. **26:** 153–184, October 1939.
9. FRAZELL, E. L.: Correlation of Calculated Tumor Doses and Five-Year Survivals in Radiation Therapy of Cancer of Cervix: Review of 136 Cases. Am. J. Roentgenol. **39:** 861–865, June 1938.
10. TOD, M. C.: Optimum Dosage in the Treatment of Carcinoma of the Uterine Cervix by Radiation. Brit. J. Radiol. **14:** 23–29, January 1941.
11. REINHARD, M. A., GOLTZ, H. L., AND SCHREINER, B. F.: Study of Radiological Treatment of Cancer of the Cervix. Radiology **39:** 144–150, August 1942.
12. ARNESON, A. N., AND QUIMBY, E. H.: Distribution of Roentgen Radiation in the Average Female Pelvis for Different Physical Factors of Irradiation. Radiology **25:** 182–197, August 1935.
13. COOPER, R. W.: Intravaginal Roentgen Therapy in the Treatment of Carcinoma of the Cervix. New Orleans M. & S. J. **91:** 445–447, February 1939.
14. REGAUD, C.: Sur les principes radiophysiologiques de la radiothérapie des cancers. Acta radiol. **11:** 455–484, 1930.
LACASSAGNE, A.: Radiotherapy of Cancer at the Radium Institute of Paris. Nelson Loose-Leaf Medicine, New York, Thos. Nelson & Sons, 1931.
15. QUIMBY, E. H.: Some Practical Considerations Regarding Various Qualities of Roentgen Rays in Therapy. Radiology **38:** 261–272, March 1942. Also: Syllabus of Lectures. The Physical Basis of Radiation Therapy. Ann Arbor, Edwards Brothers, Inc., 1939.
16. SIEVERT, R. M.: Die γ-Strahlungsintensität an der Oberfläche und in der nächsten Umgebung von Radiumnadeln. Acta radiol. **11:** 249–301, 1930.
17. WHITE, T. N., MARINELLI, L. D., AND FAILLA, G.: A Measurement of Gamma Radiation in Roentgens. Am. J. Roentgenol. **44:** 889–903, December 1940.
18. QUIMBY, E. H.: Specification of Dosage in Radium Therapy. Janeway Lecture, 1940. Am. J. Roentgenol. **45:** 1–16, January 1941.
19. FAILLA, G.: Measurement of Tissue Dose in Terms of the Same Unit for All Ionizing Radiations. Radiology **29:** 202–215, August 1937.
20. MACCOMB, W. S.: Low-Voltage Roentgen Therapy in Skin Cancer: Study on Relationship of Dosage to Size of Field. Am. J. Roentgenol. **41:** 437–440, March 1939.
21. DEAN, A. L., AND BALFOUR, J.: Treatment of Epithelial Tumors of the Bladder with Radiation. N. Y. State J. Med. **40:** 1431–1434, Oct. 1, 1940.
DEAN, A. L.: New Methods of Irradiating Bladder Tumors. Tr. Am. A. Genito-Urin. Surgeons **31:** 221–225, 1938.
22. LASNITZKI, I., AND LEA, D. E.: Variation with Wavelength of the Biologic Effect of Radiation. Brit. J. Radiol. **13:** 149–161, May 1940.
23. LEA, D. E.: Dependence of Biological Effect of Radiation on Intensity and Wavelength as Measured by Delayed Lethal Action on Chick Embryos. Am. J. Roentgenol. **45:** 605–613, April 1941.
24. MOTTRAM, J. C. AND GRAY, L. H.: Relative Response of the Skin of Mice to X and Gamma Radiation. Brit. J. Radiol. **13:** 31–34, January 1940.
25. WALKER, J. Z.: New Technique of Treatment of Carcinoma of the Cervix Uteri by Combining X-ray and Radium. Brit. J. Radiol. **13:** 1–24, January 1940.
26. TOD, M. C. AND MEREDITH, W. J.: Dosage System for Use in the Treatment of Cancer of the Uterine Cervix. Brit. J. Radiol. **11:** 809–823, December 1938.

DISCUSSION OF SYMPOSIUM ON CARCINOMA OF CERVIX UTERI

(Papers by L. R. Sante, Herbert E. Schmitz W. Walter Wasson, and Manuel Garcia)

Robert S. Stone, M.D. (San Francisco, Calif.): There are several points that I would like to bring up in connection with Doctor Sante's paper. In the first place, he advocates pneumoperitoneum as a method that can be used to get the bowel out of the way in treating cancer of the cervix. I think we must recognize, however, that when the space is filled with air instead of with bowel, the depth dose is decreased by a considerable quantity. With 200-kv. radiation dependence is placed on the scattering to build up the depth dose at 10 cm. The secondary rays account for about 40 per cent of the dose at this depth. If we remove the scattering medium, we increase the amount of primary radiation that reaches the depth but I doubt whether we build up as satisfactory a depth dose as when the bowel is present. We have, therefore, to weigh the question whether the damage to the bowel is more serious than the loss of depth dose which will result and the trouble that is involved in the procedure.

Doctor Sante mentioned that a complete absorption of the air in the abdomen requires about fourteen days and that two fillings should be sufficient to carry the patient through. If the filling lasts only fourteen days, I am sure that in the last few days of that time the bowel would not be very far out of the way, and if an attempt were made to go through without a re-fill, a great deal of the advantage he claims would be lost.

I would also like to talk about the fields that Doctor Sante suggests. He talks about using two 15 X 15-cm. fields on the pelvis, one on each side. Now the part of the pelvis that we are aiming at is the pelvic cavity, which is usually about 13 cm. wide. If we allow 4-cm. clearance in the mid-line, that is 2 cm. on each side, the center of the field, since we want the dose to reach the lateral wall of the pelvic cavity, is only 5 cm. on out. A field 10 cm. wide is therefore sufficient. With a 15-cm. field a tremendous amount of the tissue out beyond the pelvic cavity is irradiated and I would imagine that one would be likely to get more aseptic necrosis of the head of the femur.

I was interested to see the illustrations of the use of the upper fields. I don't quite see how *I* could aim at a pelvis from a field starting 15 cm. up from the pubic bone.

The use of intravaginal radiation is something with which I have had no experience, but on theoretical grounds I would wonder why one would use 200-kv. radiation when trying to get a large dose into a superficial lesion. The object of the intravaginal route is to change a deep-seated cancer to a superficial lesion and to avoid affecting other organs. With 200 kv. the depth dose is built up away beyond the point where one wants it to be. It seems to me logical that a lower kilovoltage and a lower filtration would be the method of choice.

Doctor Schmitz has brought us up to date on his use of the supervoltage machine. I think the main point of his paper, outside of his five-year statistics, is the fact that distant metastases were not so well known before radiation therapy was instituted. We have had a similar experience, which I think is due to two facts: we are keeping the patient alive longer and, as Doctor Schmitz showed, we do, with irradiation, leave some cancer encapsulated in parts of the cervix and the lymph nodes, and this can spread later if it hasn't spread before.

Doctor Schmitz mentioned that Doctor Robinson and I made no mention, in our paper, of blood-borne metastases. We were discussing there local metastases and the regions to be treated. I am sure he would not want to treat the whole body in order to get the blood-borne metastases, which spread a long way.

Doctor Wasson presents a new and unusual method of treatment which, on the surface, looks as if it has great possibilities. I think that he has stated the case well when he says it requires a very meticulous technic. Careful aiming will be necessary to avoid overlapping of fields. I don't quite see how he is going to get any more radiation into the tumor than we can already get by using, shall I say, a less meticulous method. It has seemed to me that by external irradiation plus radium we have been able to get a tolerance dose, if you wish to call it such, to the cervix and the tissues around it. These other methods may be a means of increasing the local dose and decreasing the amount we need to obtain in other ways, but, as I think has been brought out in the past many times, the cure of cancer of the cervix, even in Stages I and II, fails because there are metastases. It seldom fails because we don't control the local lesion. New methods of controlling the local lesion are of interest, but I doubt that they will add anything to our cure rate in cancer of the cervix.

Doctor Garcia has presented a most enlightening paper and one that I think will bear our close study when it is published. The figures that he juggles around so freely are a little difficult for some of us, not quite so mathematically minded, to follow, but I think that this method of attack is the one that is going to lead us to a better treatment of these lesions.

The point that he brings out, that maybe we are putting too much radiation in, going beyond what is necessary, is a very important one. We may do more harm than good by giving too much radiation. I have seen some patients who have survived five years but who have been so miserable from effects on the bowel—and I don't mean local radium burns; I mean diffuse fibrosis—that they wished they were not alive. If we can get the maximum number of cures by a lower dosage, which can be determined only by such methods as Doctor Garcia has brought forth, then I think that this method of studying the problem will have justified itself.

Conversion factors are things that a lot of men may not think much about, and yet they need to be before us all the time. A roentgen of gamma rays is one unit; a roentgen of 200-kv. x-rays is another unit, and a roentgen of 90-kv. x-rays is still a third, and conversion factors, such as have been suggested, must be used. Doctor Garcia's look as if they are as near the proper ones as we can get before we can be satisfied with totalling up the doses that are received from various sources.

Lewis G. Allen, M.D. (Kansas City, Kansas): I will discuss the papers in reverse order. Confirming the remarks of Doctor Stone, I would recommend Doctor Garcia's paper for study. He supplied me with a copy and I enjoyed it more the third time that I read it than I did the first.

It is highly desirable that the quantity of radiation, both roentgen and gamma rays, be expressed in a common unit. By such a plan, the summation of the irradiation effects at selected points in the pelvis may be computed as may be particularly indicated. Doctor Garcia repeats the warning of the physicists that, while both x-ray and gamma ray doses can be expressed in roentgens, the doses may not be simply added. Doctor Quimby has shown that the biologic effect is not a constant function of the amount of radiation when the average or effective wave length is changed.

Flexibility in the plan for irradiation of the uterine cervix and the adjacent parametria is essential. As has been repeatedly pointed out, no set technic can be expected to affect all the variations of the disease. At the same time, improvement in results must come from accurate evaluation of actual tissue dosage, and while the tendency in all irradiation therapy has been to larger doses, over-irradiation is a danger which must be considered.

Arenson, in 1936, in his description of the cervical triangle, indicated that radium could not be expected to deliver a lethal dose to a tumor located at a distance more than 3 or 4 cm. from the cervical canal—that when the area within one centimeter of the intracervical tandem received from 25 to 40 threshold erythema doses, the parametrium removed 4 cm. therefrom received but from one to four threshold erythema doses, while the bladder and rectum received as high as seven threshold erythema doses. It is manifestly true, therefore, that the region adjacent to the applicator is highly irradiated but that

the parametrial region is inadequately irradiated by intracanalicular application. It is likewise impractical to deliver large doses of roentgen radiation to patients who have already considerable destruction of tissue by radium.

The paper by Doctor Garcia is enlightening and singular, in that he has converted the computed doses to the equivalent amounts of 200-kv. x-rays. The conversion equivalents appear somewhat involved to those of us who are unaccustomed to thinking in mathematical formulae. He has included in his consideration the evaluation of the period of time consumed in the administration of irradiation dosage, and it would appear that his conversion conceptions are accurate. His essay emphasizes the assistance the physicist contributes in the treatment of malignant growth.

The matter of radioresistance and its variability remain, and since radioresistance of cervical cancer increases as the neoplasm spreads to the pelvic wall, further consideration of his totals will no doubt assist in more adequate irradiation of these areas. As he states, improved end-results are related to higher tissue doses in the areas where recurrences are more frequently noted clinically.

I am sorry that Doctor Wasson, in his discussion of intravaginal irradiation, did not include his usual warning, for I have watched him work, of the importance and the necessity of gentleness in the handling of malignant growths. I believe that intravaginal irradiation has something to contribute from the standpoint of the possible sterilization of the lesion before it is manipulated in the course of radium insertion. Perhaps that observation and Doctor Wasson's teaching are pertinent in view of the discussion of Doctor Schmitz of embolic phenomena subsequent to higher voltage therapy and perhaps it may be a warning to us that greater care in manipulation of malignant cervical cancer by the insertion of tandems and other applicators in the cervix may be the reason why (as Doctor Schmitz has pointed out) distant metastases may take place at a time somewhat removed from the time of irradiation.

I, too, had some questions about Doctor Sante's paper. First, in line with the suggestion of Doctor Stone that we are going to lose some of the irradiation effect due to scattering, have comparative measurements been made of the dosage delivered to the cervix with and without pneumoperitoneum? The other question has to do with dosage. I thought Doctor Sante said that he treated four ports anteriorly and one laterally each day and that the patient therefore received a thousand roentgens daily. Does the removal of the intestinal tract from the pelvis diminish radiation sickness to such an extent that so huge a dose as a thousand roentgens could be delivered in a single day?

Rieva Rosh, M.D. (New York, N. Y.): I, also, wanted to ask how a patient can stand a thousand roentgens a day and not have radiation sickness. Doctor Sante states that he is usually able to finish the therapy in two weeks, and he did say that one refilling of air was required. I don't know whether as much therapy as he outlines could be given in that time even at a rate of a thousand roentgens a day.

I have a question for Doctor Schmitz. With his supervoltage technic, does he notice any undesirable effect on the gastro-intestinal tract and bladder in comparison with the ordinary technic of 200,000 volts? With the larger doses we have been getting quite a number of reports of bleeding from the gastro-intestinal tract and effects on the bladder mucosa.

I have a question, too, for Doctor Wasson. He states that he has no particular trouble in placing the cylinder intravaginally. At Bellevue Hospital, in New York City, we attempted to use some intravaginal cones. Most of our patients, however, have disease of Stage III or IV and we were never able to use the direction of the portals demonstrated on his diagrams. I wonder if the cases he treated were Stage I and II cases.

Herbert E. Schmitz, M.D. (closing): I am sorry that Dr. Stone misunderstood me. I wished to say that there were emboli in the vessels of the pelvis as well as in the lymphatic spaces. He did not mention this in his paper, though that is not said in criticism.

I have not noticed any difference in the effect of 800 kv. and 200 kv. on the gastro-intestinal tract or on the bladder. The dosage that we are using gives us a very acute reaction, which subsides after treatment without any secondary effect which is greater than that we had obtained with 200 kv.

W. Walter Wasson, M.D. (closing): The question of 140 kv. or 200 kv. depends a great deal upon the size of the patient. I have used both. If the patient is a large person and there is advanced carcinoma filling the pelvis, I am quite sure that 140 kv. is not adequate. On the other hand, 200 kv. will be of distinct advantage.

This technic has not been offered as a method for supplanting the use of radium or other radiation but rather in order that the radiologist may select his approach to his problem.

Every case that comes to us I think is an individual problem. The radiologist should have at his command the machinery and the ability necessary to attack cancer as he finds it.

In my own hands, the use of radium in the cervix, in an attempt to get a uniform distribution of rays through the pelvis, produced a great deal of necrosis of the cervix and sometimes considerable infection. It has been possible by supplanting some of the dosage necessary from radium with the use of intravaginal x-rays to cut down the quantity of gamma radiation and thereby reduce the necrosis.

Doctor Allen has spoken of trauma. I think it is possible by this method to quiet down our very

malignant tumor to the point where we are safer in applying radium.

The ease with which we are able to use these cylinders depends a great deal upon the selection of the cylinder. If the case is advanced, with considerable involvement of the broad ligaments filling the pelvis, the cylinder will probably have to be a smaller one. That again depends upon the vaginal orifice. I have not had trouble in placing these cylinders.

I think the use of the air inflation is very essential. This makes it possible to unfold any of the vaginal mucous membrane, to push soft tissues out of the way, and to place the cones with greater ease.

Someone in his discussion spoke about the meticulousness of this procedure. I grant it is meticulous, but by using the cervix as a landmark, we can know at all times what region we are treating and whether or not the cone is placed properly.

Fluoride Osteosclerosis from Drinking Water[1]

JOSEPH F. LINSMAN, Major, M.C., and CRAWFORD A. McMURRAY, Major, D.C., U. S. Army

ALTHOUGH THE medical and dental professions are well acquainted with the effects of fluoride-containing drinking water on the teeth, with resulting dental fluorosis (mottled enamel) (1), the condition of osteosclerosis in the bones of human beings who have incurred mottled enamel from this source is not well known. As a matter of fact, no case of this kind has been reported in this country. The condition may have potential public health importance. Such a case is the basis for this paper.

REPORT OF A CASE

M. W. D., white soldier, aged 22, entered William Beaumont General Hospital on June 18, 1942, because of a chalazion of the upper right eyelid. The lid infection promptly subsided under treatment but, because of a rather severe anemia noted on the routine examination, the patient was detained in the hospital for further study.

On questioning, it was found that he tired easily but had no other complaints. His family history was negative for anemia. Two brothers, aged 28 and 30, were in the Army and in good health. They had spent their childhood in areas in which mottled enamel was non-endemic. One sister, aged 20, was in good health but did have moderately severe mottled enamel. She had spent her entire life in the same areas in which the patient was born and raised, in which mottled enamel was endemic. Roentgenographic study of these members of the family was negative for osteosclerosis.

The patient gave a history of measles and mumps in childhood. He had an appendectomy at the age of four and a tonsillectomy at the age of ten. At fifteen he sustained an injury to the right kidney, followed by hematuria for one week. There was no history of bleeding tendencies. There had been no contact with chemicals except for a period of three months before the patient entered the hospital, when he used kerosene and high octane gasoline in cleaning airplanes. For the past three months he had noticed some "trembling" of the hands. Since coming into the Army he had gained 23 lb. In the review of systems, no positive findings were elicited. There was no history of hematemesis, melena, or hemorrhoids.

The patient was born in Spur, Texas, where the fluorine content of the drinking water ranges up to 12 parts per million, and lived there until the age of seven years. He then moved to Post, Texas (fluorine content of drinking water 5.7 parts per million), where he lived for two years. At the age of nine he moved to Lubbock, Texas (fluorine content of the water 4.4 parts per million), where he remained for seven years. In all of these communities, he used the city water supply for drinking and cooking purposes. He then moved to Washington, D.C., where he lived for two years. At the age of eighteen he returned to Lubbock, Texas, and was there until entering the Army at twenty-one.

About five years ago the patient was troubled with easy fatigability and was seen by his local physician, who prescribed bed rest for a few days but no medication. After this he felt better. In January 1942, following an upper respiratory infection, he noticed that he began to tire easily on exertion. Blood study at that time revealed a red blood count of 3,420,000 with a hemoglobin of 75 per cent (Tallqvist).

The patient was 5 ft. 7 1/2-in. tall and weighed 144 lb. There were slight choreiform movements of the extremities and a coarse tremor of the hands. The skin and mucous membranes were pale. All the teeth showed a severe degree of mottled enamel. There were some slight acneform lesions on the nose, thighs, legs, and buttocks, and a chalazion on the right upper eyelid. The isthmus of the thyroid was barely palpable. The pulmonic second sound was accentuated, and there was a systolic murmur audible over the entire precordium. Pulse was 76 and was equal and regular. Blood pressure was 128/82. The eye grounds were negative except for pallor. The spleen, liver, and kidneys were not palpable.

For the first two weeks in the hospital, the stools were positive for occult blood but were negative for parasites or ova. During this period, however, frequent mild nosebleeds occurred. Repeated blood counts were made between June 18 and Sept. 17, 1942. The red blood cells ranged between 1,680,000 and 2,680,000, and the hemoglobin between 35 per cent and 65 per cent (Tallqvist). Slight anisocytosis was seen on the smear. The lower figures for both red cells and hemoglobin were recorded after about two months of iron and liver therapy. The white count and the differential count were normal. On two ocasions the color index was slightly below 1 and on four occasions it was above 1 (1.1, 1.2, 1.3, 1.4). The volume index (hematocrit) was 1.0 and

[1] From the Roentgenological and Dental Services, William Beaumont General Hospital, El Paso, Texas. Presented before the Radiological Society of North America, at the Twenty-eighth Annual Meeting, Chicago, Ill., Nov. 30–Dec. 4, 1942.

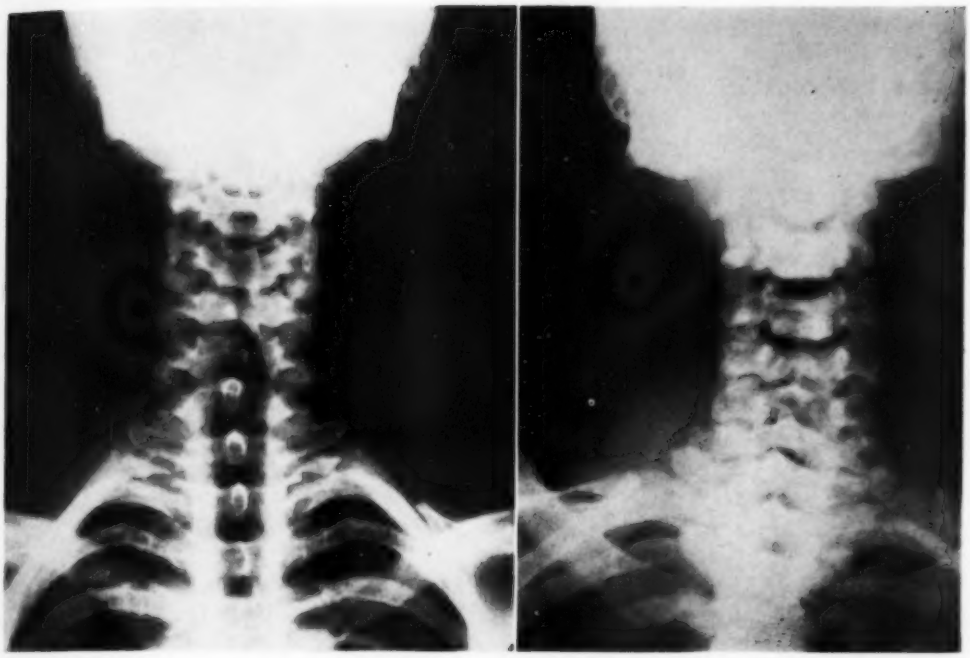


Fig. 1. Roentgenogram of a normal cervical spine (left) compared with the patient's (right). The thickened trabeculae in fluoride osteosclerosis produced a marked increase over the normal bone density.

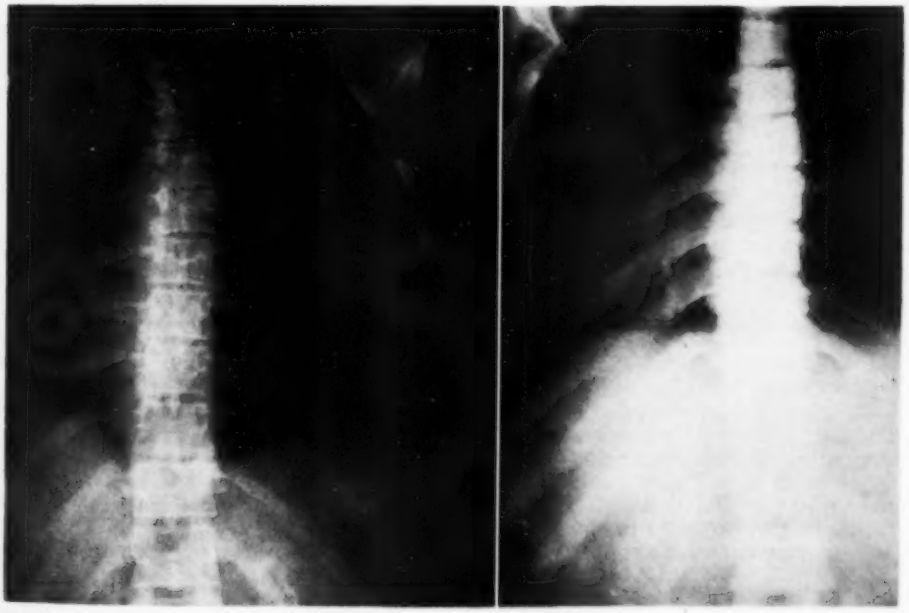


Fig. 2. A normal roentgenogram of the adult thoracic cage is seen on the left, with the patient's on the right. Notice the thickened course trabeculae; where they are too thick, the appearance is chalk-like.

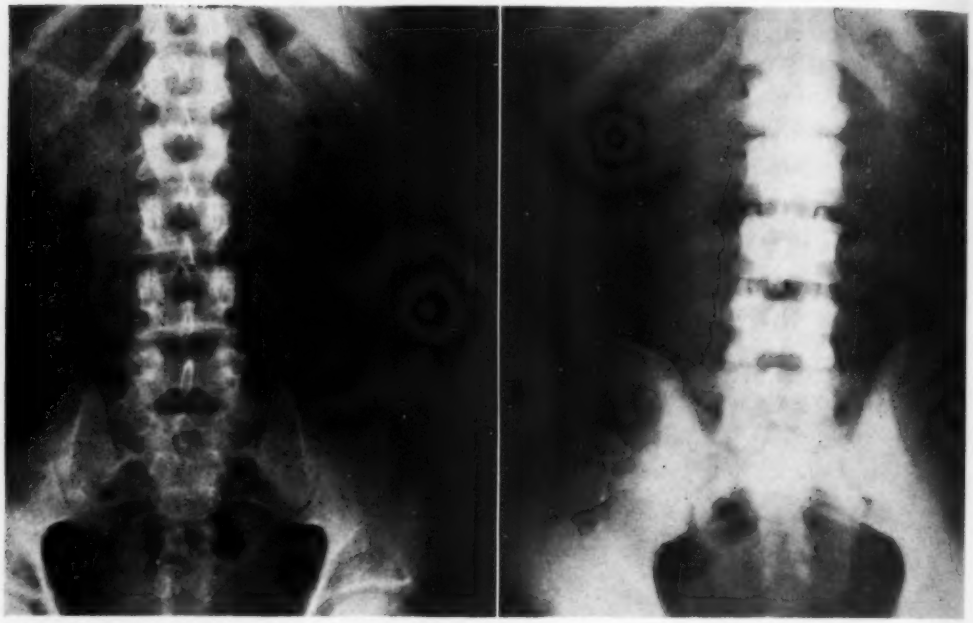


Fig. 3. Increase in density in the patient's lower ribs, lumbar spine, and pelvis (right), compared with the normal (left). The trabecular pattern is almost completely obliterated by this increased density.

1.05 on two occasions. Bleeding and clotting times were normal. The blood sedimentation rate was 35 mm. in sixty minutes. A red blood cell fragility test was normal. The icteric index of the blood serum was 5. Gastric analysis showed free acid, with the total acidity ranging from 32 to 56 and the free HCl from 12 to 20 in fractional specimens. Serum calcium and phosphorus determinations were done twice, the figures for calcium being 10.0 and 9.0 and those for phosphorus 8.2 and 8.5. Phosphatase determinations were not done. The electrocardiogram was normal. Sigmoidoscopic examination was negative. Gastroscopic examination was negative except for some slight color change in the anterior portion of the antral region, where the mucosa was more gray than normal. In the higher parts of the stomach there were definite edema and hyperemia. Urine examination on entrance showed a specific gravity of 1.003, albumin 1+, with a few white blood cells and epithelial cells on microscopic examination. The blood Kahn test was negative. A chest roentgenogram was negative. The Mosenthal kidney function test showed fixation of the specific gravity between 1.005 and 1.007, with a day to night ratio of 3 1/2 to 1. A phenolsulphonphthalein kidney function test showed no appearance of the dye in two hours.

Gastro-intestinal roentgen studies, done because of the occult blood in the stool, revealed an abnormal appearance of the bones, and a skeletal survey was therefore instituted (see Figs. 1, 2, and 3). The report was as follows: "The pelvis, the entire spine, and the thoracic cage all show marked increased density of the bony structures so that the bones have an almost chalk-like appearance. Where this increased density has not completely obliterated structural definition in these bones, their trabeculae appear thickened. Increase in density with thickening of the trabeculae is also present in the scapulae, clavicles, and in the proximal portions of both humeri. These changes are less marked here than in the bones of the trunk. The rest of the bones of the extremities show to a lesser degree some increase in density and some increase in the thickness of their trabeculae, and what appears to be a slight amount of cortical thickening so that their diaphyseal portions appear increased in caliber. The bones of the skull also show slight generalized increase in density with some thickening of the occipital bone."

Therapy, consisting of rather large doses of ferrous sulphate by mouth and liver extract intramuscularly, 1 c.c. daily, was instituted soon after admission. There was no improvement in the anemia after almost two months of treatment, and the response of the reticulocytes to the liver therapy did not exceed 2 per cent. The anemia progressed in spite of the therapeutic measures.

On Aug. 28, 1942, a biopsy of the body of the sternum was done. This showed grossly thickened trabeculae. Microscopic examination revealed dense fibrous tissue and thickened trabeculae. There was no especial osteoblastic activity, and the

marrow spaces contained abundant cellular marrow. Erythropoietic cells appeared diminished but myeloblastic cells did not.

The sternal biopsy wound became locally infected, and a chill followed by fever occurred. At this time the patient's condition was obviously bad, and he was given a 500-c.c. blood transfusion. A urea clearance test showed 6.3 per cent of average normal function. The non-protein nitrogen of the blood was 180 mg. per 100 c.c., and the urea nitrogen 83.3 mg. A urological consultation was obtained, and a catheterized residual of 1,350 c.c. of turbid urine was found. A cystometrogram showed a hypotonic neurogenic bladder. An indwelling catheter was placed in the bladder.

The patient's course was rapidly downhill. The non-protein nitrogen level of the blood increased to 300 on Sept. 4, 1942, and the CO_2-combining power of the blood dropped to 23 volume per cent. Another 500-c.c. transfusion was given, but most of the time the patient remained in a uremic coma. His blood pressure showed slight elevation for a week before death, the readings averaging 150/70. Repeated urine examinations during this period revealed albumin 1 to 3+, with a moderate number of red cells and varying numbers of white blood cells microscopically. Death occurred on Sept. 17, 1942.

Autopsy: All the teeth showed a severe degree of mottled enamel. There was a generalized pallor of all organs. One parathyroid was found and appeared to be slightly enlarged grossly. The contents of the thoracic cavity were normal. The gastro-intestinal tract, pancreas, biliary system, and spleen were normal. The right kidney was a large cystic mass, measuring 18 × 9 × 7.5 cm. Its blood vessels were normal. On incision, a great amount of thin, greenish fluid escaped. The wall of the kidney measured less than 1 mm. in thickness. It had a pale, rather opaque, smooth white lining, the pallor being interrupted by rather discrete red streaks representing congested vessels, but the congestion was not diffuse or uniform. The internal portions of this kidney showed hugely dilated calices, between which there was a small amount of uniform, pale tan tissue which presented none of the characteristics of renal substance. The extrarenal pelvis was tremendously dilated and was continuous with the right ureter, which was dilated and thin-walled. The circumference of the ureter on this side was 4.5 cm., and it was uniform down to the bladder.

The left kidney was in marked contrast to the right. Its blood vessels were normal. This kidney was very small and contracted, measuring 8 × 4 × 2.5 cm. Its ureter was moderately dilated, with uniform caliber. The ureteral circumference was 2.5 cm. The mucosa was moderately congested but essentially smooth. On incision the left kidney showed apparent complete obliteration of the cortical medullary junction. The renal substance was represented by a yellowish tan tissue in which the usual cortical and medullary striations were almost completely obliterated. There were a few irregular dots and flecks of whitish, tough tissue. The organ was strikingly pale. Its capsule was thin and stripped with considerable difficulty, leaving a slightly pitted surface. The stripped surface was smoother than one would expect from the difficulty experienced in stripping the capsule. The kidney pelvis was moderately dilated, as were the calices. The thickness of the renal substance varied from 1.0 to 1.5 cm. The pelvic mucosa was thick, white, and opaque, with rather marked congestion, but the mucosal surface seemed relatively smooth. A small amount of thin greenish fluid was present in the pelvis.

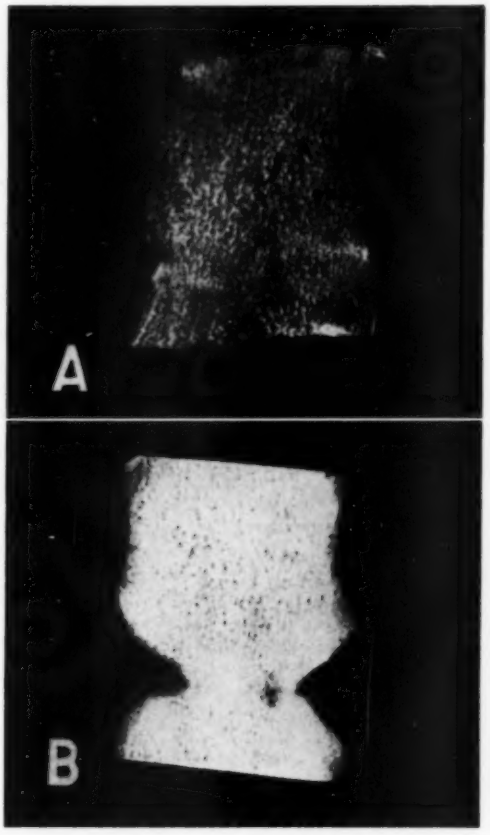


Fig. 4. Roentgenogram showing portions of (A) a normal sternum and (B) the patient's sternum. The increase in density due to the thickened trabeculae is illustrated.

No obstruction between the ureters and bladder could be demonstrated.

The bladder was not enlarged but showed thickening of its wall, principally through edema of the

mucosa. The mucosal surface was thrown up into bleb-like structures, which were considerably congested but not ulcerated. The muscular portions of the bladder were pale but of average thickness.

The prostate was small and symmetrical and showed no obstruction to urinary flow. The inferior portions were represented by multiloculated cystic spaces filled with whitish purulent-appearing fluid. The rest of the organ was normal.

The spinal cord was removed but the brain was not. The cord was not remarkable grossly.

The bone could be sawed without difficulty. It had a rather pale appearance. Trabecular markings were unusually coarse (Fig. 4). The cortex in the various specimens appeared slightly thickened and had a white, somewhat eburnated appearance. Marrow tissue was barely detectable as scanty pale red flecks.

Microscopic examination of the tissues showed essentially normal findings except in the urinary tract and osseous system, as noted below.

In the left kidney there was extensive scarring, with marked distortion of the architecture. Severe infiltrations, principally of mononuclear cells, but with abundant sprinkling of polymorphonuclears, occupied the scarred tissues. There were many completely hyalinized glomeruli with others partially hyalinized. Still others exhibited extensive fibrosis. Small adhesions to the capsule were sometimes present, but there were no epithelial crescents. In general, the capsules were greatly thickened. Large numbers of tubules were destroyed. Most of the persisting tubules showed flattened atrophic epithelium and were filled with colloid-like casts. Many tubules showed considerable dilatation. There was severe infiltration of the pelvis, lymphocytes and plasma cells predominating. The pelvis was considerably thickened by fibrous tissue. Blood vessels showed some thickening of their walls, principally of the media. Hyperplastic intimal changes were not present, but the lumens were nevertheless narrowed.

In the right kidney the changes were qualitatively the same but quantitatively different. In the very thin portions of the kidney wall, only large dilated tubules filled with colloid-like material and lined by flattened epithelium remained from the parenchymatous structures. There were no glomeruli, not even hyalinized ones. The thin wall was densely fibrous, and near the dilated pelvis there was extremely marked cellular infiltration. The lumen of the pelvis contained large masses of polymorphonuclear cells. Other portions of the right kidney showed somewhat more parenchyma, which resembled the left kidney, except for more damage and greater distortion. The sections of the right kidney all showed purulent material within the pelvis, which was lacking in the left kidney. In the pelvis there were intense cellular infiltration and edema beneath an epithelial layer that was surprisingly intact. Large mononuclear phagocytes were present in considerable numbers.

Both ureters showed thickening with extensive plasma-cell infiltration in the tunica propria and to a lesser extent through the remainder of the wall.

The prostate showed large abscesses, poorly encapsulated, within its capsule.

In the bladder sections the epithelium was not present. There was severe and extensive inflammatory infiltration with plasma cells, lymphocytes, and many polymorphonuclears.

Sections of vertebrae, sternum, and pubis were essentially similar. The bony trabeculae were definitely thickened. Cement lines were rather prominent. In a few areas there was a little osteoblastic activity, but in general this was very slight. Most trabeculae, although bounded by narrow zones of osteoid tissue, showed neither osteoblastic nor osteoplastic activity. The marrow was fairly abundant and very cellular. It appeared essentially normal in composition, although an unusual amount of granular amorphous débris was present among the cells. There was very little adipose tissue within the marrow.

Portions of the sternum (body) and a lumbar vertebra (body) were analyzed for their fluorine content along with normal bones as controls. The sternum contained 0.69 per cent fluorine in the bone ash, while in the lumbar vertebral body there was 0.75 per cent in the bone ash. The control analyses were satisfactory and showed no fluorine with the method employed (9). The patient's lower left bicuspid teeth were also analyzed for fluorine; they contained 0.45 per cent in their ash. Normal control teeth showed no fluorine.

Specific gravity determinations on a portion of the patient's pubis as compared with a normal control were as follows: Normal pubis 1.838; patient's pubis 2.196. These determinations were made on defatted bone by weighing bone sections in air and in water. The bones were soaked in water for seventy-two hours before their second weighing. Results are based on distilled water at room temperature.

The *pathological diagnoses* were: chronic bilateral pyelonephritis; acute right pyonephrosis; bilateral hydroureter with ureteritis; acute cystitis; abscesses of the prostate; sclerosis of bones (due to chronic fluoride intoxication) and dental fluorosis; hyperplasia of bone marrow.

DISCUSSION

History of the Subject: Drinking water was first assumed to be the cause of mottled enamel by McKay (2) in 1916. Proof that a high fluorine content of the water is the cause of mottled enamel (3) and its importance as a health problem (4) have been well established, and innumerable articles dealing with the cause and prevention of the condition have been published.

Greenwood (5) has recently reviewed the literature from 1933 to 1939 on fluoride intoxication, and he cites the experimental findings of others in chronic fluoride poisoning. Animals which have ingested repeated small doses of fluorine salts store these salts in the body with eventual chronic fluorine poisoning. At autopsy their bones are characterized by increased thickness, loss of normal color, presence of exostoses, and increased fragility.

Human cases of fluoride osteosclerosis of other origin than drinking water have been reported by Møller and Gudjonsson (6) and Roholm (7) in cryolite miners. These writers described widespread osteosclerosis of the bones with osteophytic formation at the attachments of ligaments, tendons, and periosteum. Cryolite is a double fluoride of sodium and aluminum, containing as much as 54 per cent of fluorine. Møller and Gudjonsson's patients with the most extensive bone changes showed an anemia with a low red cell count and a high hemoglobin content. Bishop (8) reported the same bone changes in a laborer who had been exposed for eighteen years to the dust of a fertilizer made by crushing phosphate rock which had a high fluorine content (3.88 per cent). His patient showed sclerosis of the entire skeleton except the skull, as well as vertebral osteophytes and calcification of the attachments of some of the ligaments. The teeth of this patient, though very brittle, did not show the characteristics of mottled enamel (9). No evidence of mottled enamel will be found unless the patient has ingested fluorine during the formative period of tooth enamel (birth to eight years of age). Mottled enamel, therefore, will not necessarily be found among industrial workers coming in contact with fluorine compounds. In Bishop's case there was no anemia. His patient died of syphilitic heart disease and was autopsied. Wolff and Kerr (9) chemically analyzed the bones of Bishop's patient and found an increase of fluorine up to 20 times the normal value, unequally distributed in the skeleton, the fluorine content being highest in the vertebrae and lowest in the long bones.

Wilkie (10) reported two cases of fluoride osteosclerosis, one secondary to exposure to hydrofluoric acid fumes over a long period and the other secondary to exposure to fluorine during the preparation of aluminum fluoride over an interval of three and a half years.

Foreign observers (cited by Greenwood, 5) have reported fluoride osteosclerosis due to continued consumption of drinking water of high fluoride content in North Africa, India, and Argentina. Spéder (11), who studied 7 persons with bad teeth living in the phosphatic regions of Morocco in Northern Africa, where there is considerable concentration of fluorine in the water, soil, and dust, found osteosclerosis in all of them. He concluded that generalized osteosclerosis is not a rare condition if one considers persons subjected to chronic fluorine intoxication.

Public Health Aspects: Mottled enamel is cosmetically not desirable. From the health standpoint, however, there is evidence that the affected teeth are less likely to become carious than normal teeth, and in most cases the stain can be removed (12). The action of fluorine in limiting dental caries was recently reviewed and analyzed by Volker and Bibby (13). Osteosclerosis due to fluorine does not appear to have any such virtue. Fluoride osteosclerosis may be dangerous because of the possibility of anemia, which may be present in this condition just as it is in osteopetrosis (marble bones, Albers-Schönberg disease, osteosclerosis fragilis generalisata). Unfortunately the sclerotic changes occur, for some reason, primarily and most severely in the bones in which most of the blood is normally formed.

This danger from drinking water of high fluorine content has been realized. In 1941, Hodges, Fareed, Ruggy, and Chudnoff (14) studied the problem of osteosclerosis in two areas in Illinois in which mottled enamel was endemic. They investigated communities where the content of fluorine in the drinking water was under

three parts per million. They found no roentgenographically demonstrable sclerosis of the skeleton in 86 subjects in one area, though these persons had been exposed to fluorides in the water for as long as sixty-one years. In the other area, 31 subjects who had constantly used the water supply from eighteen to sixty-eight years showed no demonstrable sclerosis of bone. The authors concluded that search for skeletal sclerosis should be continued in areas where the drinking water contains over three parts per million of fluorine to determine the incidence of skeletal sclerosis should be instituted as a public health measure. In positive cases, blood studies for anemia should be performed.

Pathogenesis of Fluoride Osteosclerosis: The percentage composition of fluorine is greatest in the bones showing the greatest increase in bone density in roentgenograms. The fluorine may be deposited in these bones as a calcium or magnesium fluoride (9). It has been demonstrated that in mottled teeth the fluorine content is greatly increased (13). The reason that the bones of the trunk contain more fluorine than the long bones is probably due to the greater metabolic activity in bones in which hemopoiesis is taking place. The fluoride deposition in the bone gives rise to an overgrowth of the bone trabeculae due probably to irritation (16). With thickening of the trabeculae, the resultant increase in radiographic opacity occurs.

The thickened trabeculae may encroach upon the blood-forming marrow and give

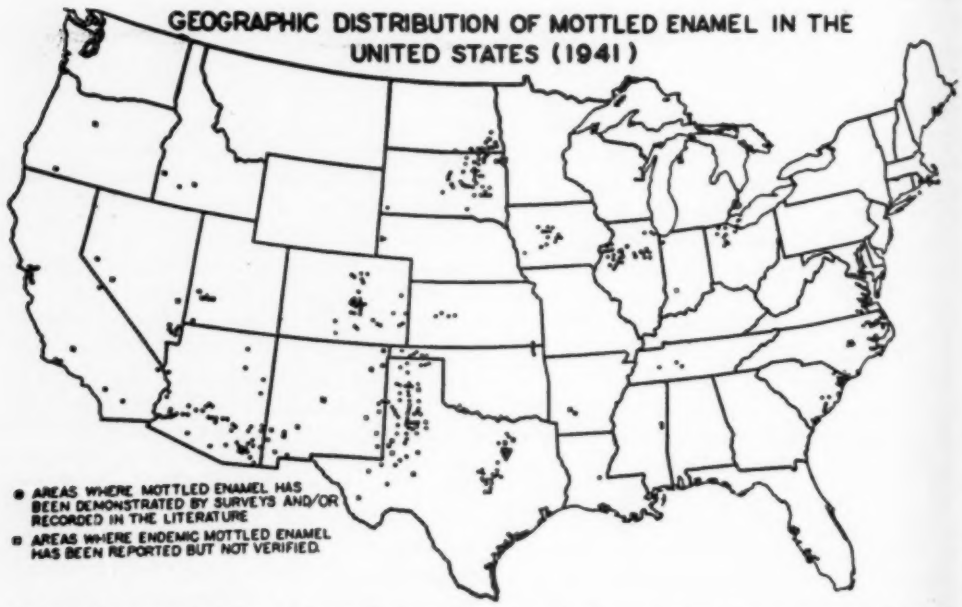


Fig. 5. Geographic distribution of endemic fluorosis in the United States. From *Fluorine and Dental Health*, by H. T. Dean, published by American Association for the Advancement of Science, 1942.

American communities in which the fluoride content of the drinking water exceeded three parts per million.

The geographic distribution of dental fluorosis (mottled enamel) in the United States in 1941 is plotted in the map in Figure 5, taken from Dean (15). Drinking waters containing 1 part per million or more of fluoride appear to be most prevalent in the middle western and southwestern parts of the United States. The condition is present in approximately 400 areas in 28 states of the United States. (15). Systematic radiological surveys of those areas where the drinking water con-

rise to an anemia from which recovery would be poor. It is because of this fact that the condition of fluoride osteosclerosis may be dangerous.

Our patient's bones had a higher specific gravity than those of a normal control. This is not in agreement with the findings of others (9), who have observed a decreased specific gravity in fluoride sclerosis of bone.

Roentgenographic Findings and Differential Diagnosis: In osteosclerosis due to chronic fluoride intoxication, the roentgenograms of the involved bones show a considerable increase in the density and coarseness of the trabecular patterns; where the density has become great enough, these patterns are obscured and the bones take on a chalk-like appearance. Bishop (8) reported long bone involvement in which there was both periosteal and endosteal thickening with the result that the outside diameter of the shaft was increased and the medullary cavity was reduced in caliber. In many parts of the skeleton the surface of the bone was irregular and extended into the neighboring ligaments. Osteophytes were present on the vertebral column. In our case, the osteosclerotic changes were particularly severe in the pelvis, vertebral column, ribs, and sternum. The bones involved were similar to the ones involved in cases reported by most other observers. Our patient, however, did not show osteophytes or calcification of tendons and ligaments. Spéder (17) states that persons up to the age of twenty-five show only the osseous change; the osteophytic changes become more pronounced in the later age groups.

In the differential diagnosis one must think of osteopetrosis (marble bones), metastatic cancer, and Paget's disease. Osteopetrosis is usually hereditary and present at birth or in infancy. Some authors have reported cases of idiopathic generalized osteosclerosis (18, 19). Freedman (19) analyzed a sternal biopsy specimen from his patient and ruled out fluorine as a cause. The diagnosis of the type of osteosclerosis is easy if one finds that the patient has endemic dental fluorosis. This finding should be present if the osteosclerosis is due to the regular consumption of drinking water of high fluorine content during the first seven years of life, when the calcification of the permanent teeth is occurring. Osteophytes and plate-like exostoses where tendons and ligaments are attached occur in long-standing cases of fluoride osteosclerosis but not usually in the other conditions. Above everything else in the diagnosis, the history of long residence in an area of endemic fluorosis or of chronic exposure to fluorides is all-important.

Comment on Case: Our patient lived his entire life, with the exception of three years, in areas where the concentration of fluorine in the water is excessively high. Considerable damage was done to his permanent tooth enamel. Similarly the skeletal changes showed the effects of the chronic fluoride intoxication.

Continuous residence in an area of endemic fluorosis from childhood for more than 15 years was found necessary to produce bone lesions in South India (20). Shortt *et al.* (21), who also studied cases of fluorine intoxication in India, found that people consumed water of high fluorine content for thirty to forty-five years before clinical symptoms of bone changes and kidney damage occurred.

The patient's anemia was striking and of great interest. During the early period of observation it was thought to be secondary to the fluorosis of the bones. The occult blood in the stools during the first two weeks in the hospital was probably due to epistaxis. Because the osteosclerosis was present where it could displace a large part of the hemopoietic system, it was considered that the anemia was due to a mechanical crowding by osseous deposit. Chapman (18) has reported two cases of severe osteosclerotic anemia in which anti-anemic therapy evoked no improvement presumably for this reason. In his cases the sternal bone marrow revealed aplasia of hemopoietic elements. Our case, however, showed abundant cellu-

lar marrow in spite of the thickened bony trabeculae.

Prior to the necropsy the renal impairment was also considered to be due to the chronic fluoride intoxication. It was felt that the kidney damage had augmented the anemia. Renal impairment could explain the high blood phosphorus recorded on two occasions, because of phosphorus retention. It is otherwise difficult to explain the absence of the usual reciprocal relation between blood calcium and phosphorus.

The sternal biopsy was the first thing to cast doubt on the clinical conception of the etiology of the anemia. The renal findings did not attract attention until relatively late in the course of the disease. At autopsy the essential pathological lesions were in the genito-urinary system. The hugely dilated kidney on the right and the bilateral hydroureter could not be explained anatomically. The pyonephrosis probably followed the local infection at the sternal biopsy site which provided a portal of entry.

The fluorine may have played some role in the anemia, but it must be concluded on the basis of the pathological findings that the anemia and its lack of response to therapy were primarily on the basis of the uremia present.

The chronic fluoremia may have aggravated existing kidney lesions. Or it is entirely possible that, because renal impairment was present, the osteosclerosis developed as a result of fluorine retention.

Data on kidney damage are limited. In severe chronic fluoride intoxication kidney damage has been reported in experimental animals (22) and in man (21). Shortt *et al.* (21) reported renal impairment in the majority of their cases of fluoride osteosclerosis from drinking water in India. It has been shown that in pigs on a ration containing 1 per cent rock phosphate (containing about 3.5 per cent fluorine) degeneration of the epithelium and convoluted tubules with a fibrosis of the kidneys occurred (22).

Apparently the severity of the tooth, bone, and other damage due to chronic fluoride intoxication depends not only on the duration and quantity of fluorine exposure but also on the intake of other necessary components of the diet such as calcium, phosphorus, and vitamins (20).

SUMMARY AND CONCLUSIONS

1. A case of osteosclerosis, exhibiting in addition mottled enamel, severe anemia showing no response to anti-anemic therapy, and bilateral renal lesions, is reported.

2. The diagnosis of fluoride osteosclerosis was proved by the history of a long residence in areas of endemic fluorosis and by fluorine analysis of the patient's bones and teeth.

3. Osteosclerosis may be a dangerous sequel to the chronic ingestion of fluorine-containing water supplies, since it may give rise to a secondary anemia due to encroachment upon the blood-forming marrow. There is also the possibility of kidney damage due to the chronic fluoremia.

4. Areas in the United States in which dental fluorosis exists and where the fluorine content of the drinking water is over three parts per million should be systematically studied by the public health authorities to determine how widespread the condition of osteosclerosis is.

5. All patients with dental fluorosis and anemia and/or signs of renal impairment should have radiographic examinations of the skeletal systems to rule out the existence of fluoride osteosclerosis.

ACKNOWLEDGMENTS: The authors are indebted to 1st Lieutenant La Monte A. Tucker, Sanitary Corps, U. S. A., for the chemical analyses for fluorine in the patient's bones and teeth and for the specific gravity determinations on the bones. We wish, also, to thank Major Harry F. Wechsler, Medical Corps, U. S. A., for his interest and suggestions.

Headquarters, 64th Medical Training Battalion
Camp Barkeley, Texas

REFERENCES

1. MCMURRAY, C. A.: Mottled Enamel. Texas Dent. J. **53:** 10–16, November 1935.

DEAN, H. T.: Chronic Endemic Dental Fluorosis. J. A. M. A. **107:** 1269–1273, Oct. 17, 1936.

SMITH, MARGARET C., LANTZ, EDITH M., AND SMITH, H. V.: Cause of Mottled Enamel, a Defect of Human Teeth. University of Arizona Tech. Bull. No. 32, 1931.

2. MCKAY, F. S., in collaboration with BLACK, G. V.: Investigation of Mottled Teeth. Dent. Cosmos **58:** 477–484, May; 627–644, June; 781–792, July; 894–904, August, 1916.

3. MCKAY, F. S.: Mottled Enamel; Prevention of Its Further Production through a Change of the Water Supply at Oakley, Idaho. J. Am. Dent. A. **20:** 1137–1149, July 1933.

DEAN, H. T., MCKAY, F. S., AND ELVOVE, E.: Mottled Enamel Survey of Bauxite, Ark., 10 Years after Change in Common Water Supply. Pub. Health Rep. **53:** 1736–1748, Sept. 30, 1938.

4. MOULTON, F. R. (editor): Fluorine and Dental Health. American Association for the Advancement of Science, Washington, D. C., 1942.

5. GREENWOOD, D. A. Fluoride Intoxication. Physiol. Rev. **20:** 582–616, October 1940.

6. MØLLER, P. F., AND GUDJONSSON, S. V.: Massive Fluorosis of Bones and Ligaments. Acta radiol. **13:** 269–294, 1932.

7. ROHOLM, K.: Fluorine Intoxication. London, H. K. Lewis and Co. Ltd., 1937. Cited by Greenwood (5).

8. BISHOP, P. A.: Bone Changes in Chronic Fluorine Intoxication; a Roentgenographic Study. Am. J. Roentgenol. **35:** 577–585, May 1936.

9. WOLFF, W. A., AND KERR, ELIZABETH, G.: Composition of Human Bone in Chronic Fluoride Poisoning. Am. J. M. Sc. **195:** 493–497, April 1938.

10. WILKIE, J.: Two Cases of Fluorine Osteosclerosis. Brit. J. Radiol. **13:** 213–217, June 1940.

11. SPÉDER, E.: L'ostéopétrose généralisée ou 'marmoskelett" n'est pas une maladie rare; sa fréquence dans l'intoxication fluorée. J. de radiol. et d'électrol. **20:** 1–11, January 1936. Abst. in Am. J. Roentgenol. **38:** 506–507, September 1937.

12. MCMURRAY, C. A.: Removal of Stains from Mottled Enamel Teeth. Texas Dent. J. **59:** 293–296, September 1941.

13. VOLKER, J. F., AND BIBBY, B. G.: Action of Fluorine in Limiting Dental Caries. Medicine **20:** 211–227, May 1941.

14. HODGES, P. C., FAREED, O. J., RUGGY, G., AND CHUDNOFF, J. S.: Skeletal Sclerosis in Chronic Sodium Fluoride Poisoning. J. A. M. A. **117:** 1938, Dec. 6, 1941.

15. DEAN, H. T.: Geographical Distribution of Endemic Dental Fluorosis (Mottled Enamel), in Fluorine and Dental Health (4), pp. 6–11.

16. HODGES, P. C., PHEMISTER, D. B., AND BRUNSCHWIG, A.: Roentgen-Ray Diagnosis of Disease of Bone, Chapter VI, Vol. I, Diagnostic Roentgenology, Ross Golden, Editor, Thomas Nelson and Sons, New York, 1941, p. 560 G.

17. SPÉDER, E.: L'ostéopétrose de la fluorose phosphatique de l'Afrique du Nord. Bull. et mém. Soc. de radiol. méd de France **24:** 200–207, March 1936. Abst. in Am. J. Roentgenol. **38:** 507–508, 1937.

18. CHAPMAN, E. M.: Osteosclerotic Anemia. Am. J. M. Sc. **185:** 171–177, February 1933.

19. FREEDMAN, E.: Advancing Osteosclerosis of Unknown Etiology; Roentgenological Manifestation of a Probable Infectious Process of Bone. Radiology **30:** 225–231, February 1938.

20. PANDIT, C. G., RAGHAVACHARI, T. N. S., RAO, D. S. AND KRISHNAMURTI, V.: Endemic Fluorosis in South India. Study of the Factors Involved in the Production of Mottled Enamel in Children and Severe Bone Manifestations in Adults. Indian J. M. Research **28:** 533–558, October 1940.

21. SHORTT, H. E., MCROBERT, G. R., BARNARD, T. W., AND NAYAR, A. S. M.: Endemic Fluorosis in Madras Presidency. Indian J. M. Research **25:** 553–568, October 1937. Cited by Greenwood (5).

22. KICK, C. H., BETHKE, R. M., EDGINGTON, B. H., WILDER, O. M., RECORD, P. R., WILDER, W., HILL, J. T., AND CHASE, S. W.: Bull. Ohio Agric. Exper. Sta. 558, 1935. Cited by Greenwood (5).

DISCUSSION

Paul Hodges, M.D. (Chicago, Illinois): Physicians who live in regions where there is a high concentration of fluorides in the drinking water should be on the lookout for cases like the one that has been reported by Major Linsman. We expected to find such cases in the coal-mining regions of Illinois and assume that we failed simply because the concentration of fluoride was not quite high enough.

All over the United States fluorides are being added to human diets. For example, fluorides are used in fruit sprays, where they are mixed with casein and other binders to hold them on the fruit in spite of rain. These binders work so well that the fluorides continue to stick in spite of rather vigorous washing of the marketed fruit. The crushed phosphate rock which is applied to agricultural land and fed to farm animals usually contains fluorides as an impurity. Most of us, therefore, ingest a good deal of fluoride regardless of where we live. If it can be confirmed by studies like those of Doctor Linsman that the ingestion of more than a trace of fluoride is a dangerous thing, then perhaps something can be done about the wholesale unnecessary feeding of fluoride to consumers of fruit and of other agricultural products.

H. L. Wilder, M.D. (Pampa, Texas): I live in a section of Texas where we have this fluoride water, and we see a number of children and adults with mottling of the teeth. I should like to ask about the possibility of an associated endocrine condition, since we see some adults who, though they have always lived in these sections, show no fluoride effects.

W. Edward Chamberlain, M.D. (Philadelphia, Penna.): One wonders, of course, why the siblings of the patient did not have osteosclerosis. The fact that the bones were proved to contain fluorine is most important, especially from the point of view of differential diagnosis. Renal rickets was not mentioned in the latter connection, but we do see osteosclerosis due solely to renal impairment with an exactly similar roentgen picture. This possibility should, I believe, be added to the list of conditions to be differentiated.

Will Major Linsman tell us whether fluorine salts were found in excessive amount in the bones at necropsy?

William T. Clark, M.D. (Janesville, Wis.): I should like to ask if there is any explanation of the lack of response to liver and iron.

Major Joseph F. Linsman, M.C. (*closing*): The endocrine glands probably play no part in dental fluorosis. The reason that mottled enamel is not

seen in adults who move into areas in which mottled enamel is endemic is that the teeth changes occur only if there has been exposure to heavy fluorine concentration in the drinking water during the first seven years of life, when permanent tooth enamel is forming.

Doctor Chamberlain asked why the siblings of our patient showed no osteosclerosis. The two brothers during the early period of their lives did not live in an area in which mottled enamel was endemic. Why the sister, who did live in such an area, and had mottled enameled teeth, showed no bone change, I do not know. It is likely that the reason our patient retained fluorine in his bones was that he had renal damage of long standing; without this the osteosclerosis might not have developed.

The analysis of the bones for fluorine was, of course, what proved this case. The patient's sternum and a vertebra were analyzed for fluorine content, and sufficient fluorine was present to establish the case as one of fluoride osteosclerosis.

I believe that the reason liver and iron therapy evoked no response in our patient was that he had such a severe uremia during his entire course in the hospital that his blood system couldn't respond. There was no crowding out of the hemopoietic system.

The dental profession has long been interested in mottled enamel due to fluorine intoxication, but the problem is primarily one for the medical profession to run down, since apparently we can get systemic effects from chronic fluoride intoxication.

The Infected Lung Cyst[1]

LEO G. RIGLER, M.D.

University of Minnesota, Minneapolis, Minn.

THE VOLUMINOUS literature on cystic disease of the lung has been thoroughly reviewed in many previous publications (1, 3, 5, 15, 16, 19, 20, 21, 24). The heterogeneous nature of the various processes included under this general title is indicated by the more than twenty terms which have been used to designate the condition (17). It has been well described by Bruce (3) and Diamond and Durham (7).

Cysts of the lung may be either congenital or acquired, bronchial or parenchymal in origin, single or multiple. They may contain fluid, gas, or both, and are often designated as non-inflammatory, although they may be the sequel of an inflammatory process and they may become secondarily infected.

The major portion of the studies on this subject have been devoted to the questions of classification (2, 21), etiology (18, 21), congenital or acquired origin (1, 2, 16, 27), and the mechanics of development of these pockets in the lung (13, 16, 26).

Two decades ago lung cysts were regarded as something of an academic problem, being considered rare, of relatively little clinical significance, and not susceptible to therapeutic procedures. With increasing knowledge, the importance of their recognition has been more generally appreciated. The frequency with which cysts of the lung are found in routine examinations of the chest under various conditions indicates that these are not uncommon phenomena and should be considered in the differential diagnosis of any pulmonary process. Furthermore, the striking advances in thoracic surgery during the past decade have made it possible to institute genuinely curative procedures, so that the importance of diagnosis has been greatly enhanced.

In 1940, Maier and Haight (15) described another and more immediately practical aspect of the problem of cysts of the lung; namely, their relationship to chronic pulmonary suppuration. Eloesser (10) had previously reported a number of cases in which infected lung cysts had been mistaken for other types of pulmonary suppurative processes. Bruce (3) likewise emphasized this possibility. Maier and Haight (15) elaborated upon this and stressed the utility of obtaining a biopsy from the wall of any pocket of fluid in the chest, to be accomplished during the institution of drainage. By this means the exact nature of the pathologic process can best be determined.

The true lung cyst, developing as it does from a bronchial bud, is commonly lined with bronchial epithelium. This is a secreting mucous membrane and the cyst will, therefore, be filled with fluid. If a communication with the bronchus exists, both gas and fluid will be found in the pocket. In some instances the communication with the bronchus is of such a nature as to cause a complete filling of the pocket with air. Apparently the secreting membrane is insufficient to produce much fluid, so that gas alone may be present. In most true cysts fluid is also found.

The bronchial communication may open or close, so that at different times the cyst may contain fluid alone or both fluid and gas. The observation of such a development is well demonstrated in the following case.

CASE 1: E. V., a male, aged 28, was admitted Jan. 11, 1942, complaining of a dry cough and pain in the left chest. In December 1941 he experienced recurrence of a sore throat which he thought had

[1] From the Department of Radiology and Physical Therapy of the University of Minnesota and the University Hospitals, Minneapolis, Minn. Presented before the Radiological Society of North America, at the Twenty-eighth Annual Meeting, Chicago, Ill., Nov. 30–Dec. 4, 1942.

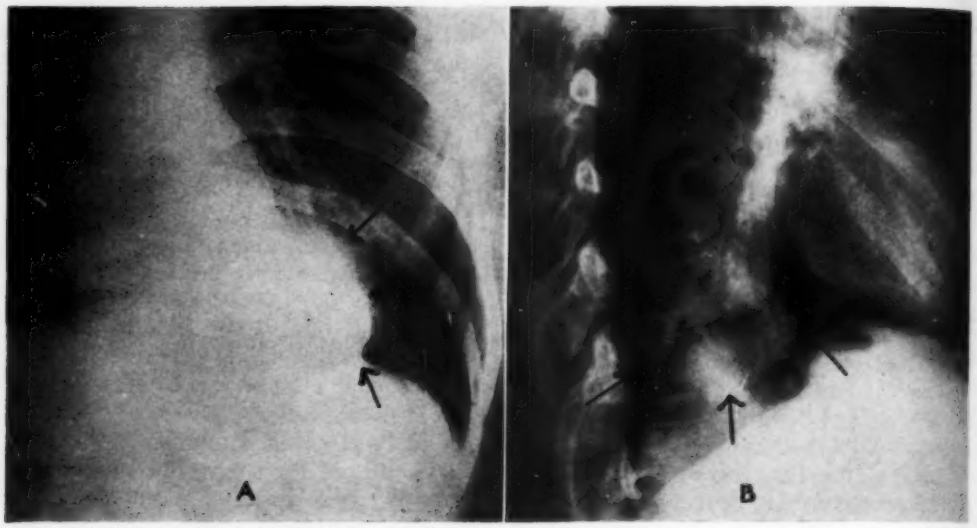


Fig. 1. Case 1: Cyst of the lung without infection. A. Sharply rounded, well defined dense shadow just lateral to the apex of the heart. No gas is shown within it. Roentgenogram made Jan. 12, 1942.
B. Lateral view, after institution of pneumothorax, showing mass within the lung, collapsing away from chest wall, but lying well behind the heart and distinct from it. Roentgenogram made Jan. 13, 1942.

produced a chronic dry cough for the past eight years. This attack lasted but a few days and the patient again was in good health. Ten days before admission he noticed a gradually developing pain on the left side. The pain was constant and had no relationship to activity or deep breathing. There had never been any dyspnea, hemoptysis, dysphagia, or expectoration. General malaise had been present for the past two months. The local physician had made an x-ray examination and found a large mass at the base of the left lung, the exact nature of which was not apparent. The past history was essentially negative.

Physical examination revealed dullness over an area from the 7th to the 10th rib posteriorly, approximately 8 cm. in diameter. There were increased breath sounds, bronchial breathing, decreased vocal fremitus, and moist râles over this area. Otherwise the physical findings were of no significance.

X-ray examination showed a large, round, sharply defined mass in the base of the left lung, lying somewhat posterior, displacing the diaphragm downward. The remainder of the lung field was entirely clear, as was the right side. In the postero-anterior view (Fig. 1A) the appearance suggested a pleuro-pericardial cyst, but in the lateral view the mass was seen to be entirely separate from the heart. Because of the possibility of an extrapulmonary tumor, pneumothorax was instituted. The mass collapsed away from the posterior chest wall with the lung (Fig. 1B). Examination two days later showed gas within this mass with a definite fluid level (Fig. 1C). The diagnosis of lung cyst with a bronchial communication was made. Repeated examinations prior to the pneumothorax had disclosed no evidence of gas in the cyst.

On Jan. 15, 1942, the thorax was opened by Dr. John R. Paine, and the lung cyst was found at the site reported. It was beneath the visceral pleura and connected with the lung at only one point, where it communicated with a very small bronchus. The cyst was dissected out and the fistula closed. Only a segmental pneumonectomy was done, the cyst being sharply distinct from the remainder of the lung. The patient made an uneventful recovery and has since been entirely well.

Examination of the excised specimen was made by Dr. Robert Hebbel. It consisted of a collapsed cystic structure which, when partly distended with fluid, measured 8 cm. in diameter. There was a small opening about 8 mm. in diameter at one point. The wall was thin; the lining was smooth, and in a few areas trabeculated. Microscopically the wall was seen to be fibrous, showing some lymphocytic infiltration; it was lined by a typical pseudo-stratified columnar epithelium characteristic of lung cyst.

Comments: The x-ray findings in the foregoing case were characteristic. The sharp outline of the pocket, the absence of other evidences of inflammation, the normal position of the mediastinum and diaphragm, all pointed to a lung cyst. Because of the juxtaposition to the heart

in the postero-anterior view, the possibility of a pleuro-pericardial cyst was considered, but the posterior location of the mass ruled this out. The demonstration of the intrapulmonary position of the mass and its bronchial communication, after pneumothorax, clinched the diagnosis.

It is to be observed that there was little or no evidence of chronic lung suppuration in this patient's history. It is impossible to determine whether or not a communication with the bronchus had been present at any previous period, although the history of a cough is suggestive. It seems highly probable that the compression of the cyst by the pneumothorax caused the bronchial orifice to open, following which gas could be observed within the pocket. The conditions leading to an infected lung cyst were thus established. In this instance extirpation of the cyst was promptly undertaken and the fluid found within it was not infected. This case also illustrates with what relative ease and safety such a condition can be cured by a competent thoracic surgeon.

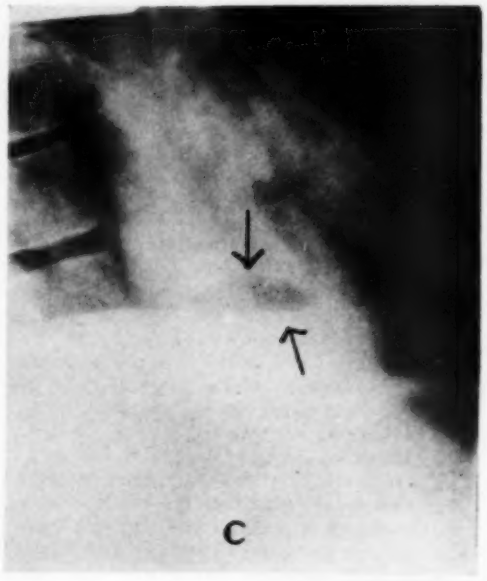


Fig. 1. C. Case 1: Oblique view, 36 hours after institution of pneumothorax (Jan. 14, 1942). The cyst is shown and within it (arrows) a gas bubble with fluid level, indicating a bronchial communication.

That the presence of a bronchial communication may lead to the development of infection within a cyst is clear. A pocket lined with a membrane secreting mucin may be entirely harmless until the entrance of infection from the general respiratory tract through a bronchial fistula. A relatively harmless cavity is, thereby, converted into a suppurative pocket which may give all the symptoms and signs of a chronic lung abscess or an encysted empyema.

The presence of a pocket of fluid and gas in the thorax may readily be detected by roentgen examination, but the determination of the nature of the process involves somewhat greater difficulty. Given a history suggestive of pneumonia and a relatively peripheral, well encapsulated pocket of fluid, a diagnosis of encysted empyema is very likely to be made. If gas is also present, the possibility of a pulmonary abscess or of an encysted empyema with a bronchopleural fistula will be considered. Thoracentesis may be done under these conditions and reveal pus, with or without living bacteria. In any such case the diagnosis of infected lung cyst should also be considered, as its roentgen appearance, considered casually, may exactly simulate either of the above conditions.

When there is added to the above considerations a history of repeated pulmonary infections, usually considered to be repeated attacks of pneumonia, or a history of repeated drainages of the pocket of fluid, either intercostal or with rib resection, without a permanent result, the possibility of some other process must always be borne in mind. Such conditions as actinomycosis or other fungus infections are well known; they usually can be excluded by bacteriological study. The exclusion of a lung cyst is much more difficult and can best be made by biopsy at the time of drainage. The following case illustrates well such a situation and the advantages of microscopic examination of tissue from the wall of the pocket.

CASE 2: P. K., a 2 1/2-year-old boy, had become ill in January 1941, at the age of nine months, with a high fever and other signs suggestive of pneumonia. Sputum examination showed type III pneumococci. The infection did not clear up in the usual fashion, although the child was treated with one of the sulfonamide compounds; several weeks later the physician caring for him thought an empyema had developed. Rib resection was done, pus was obtained, and the cavity was irrigated. Over a seven-week period drainage was effected with repeated irrigations, but a thick yellowish pus was still draining when the child left the hospital. In the next year and a half the drainage area closed several times, but again reopened.

One week before entrance into this hospital, on Aug. 28, 1942, there was a return of fever, rapid respiration, and cough, and the patient began raising a foul smelling sputum for the first time. He was taken to a local physician, who reopened the closed wound in the thorax, and the following day there was considerable drainage. Since that time the drainage had been profuse, with a noticeable odor. There was no history of any other illness.

Physical examination showed only some dullness and relatively diminished breath sounds in the lower two-thirds of the right chest. The temperature at this time was a little over 100° F. and seldom went above 102° F. The leukocyte count was 9,600, with a moderate secondary anemia. The laboratory findings otherwise were of no great significance.

The first roentgen examination (Fig. 2A) was made by the local physician on Jan. 29, 1941, shortly after the onset of illness. Multiple pockets of fluid and gas appear in the right lung. The lower pocket (arrow) protrudes over the dome of the diaphragm, which is displaced downward. The heart is displaced to the left. The process is clearly expansile.

The second examination (Fig. 2B) was made nineteen months later and shows the resected rib. The multiple pockets of fluid and gas are again shown, with fairly thick walls. Upright postero-anterior and lateral views (Fig. 2C and D) show some of the pockets to be thin-walled; there are multiple fluid levels and the expansile character of the pockets is well shown. The sharp outline of the cavities and their separation from the lung tissue are notable.

Because of the roentgen findings, the diagnosis of infected lung cyst, lung abscess, or multiple encapsulated empyemas was considered. On Sept. 23, a fragment of the ninth rib, at the site of the previous drainage, was removed by Dr. Clarence Dennis. A cavity was readily entered, and the exploring finger revealed a circular pocket too deep to be reached in its medial and upper margin. Lung tissue could be felt inferiorly and also apparently between the pocket and the chest wall on all sides of the point of drainage. Dependent drainage, so far as possible, was effected. Further palpation revealed strands of tissue stretched across the interior of the cavity, characteristic of lung cyst. Air bubbles could be made out extending into the cavity, indicating the obvious bronchial fistula.

A segment of the lining of the cavity was removed for biopsy. Microscopic examination by Dr. J. C. McCartney showed in part compact fibrous tissue and in part irregular, glandular, cyst-like areas lined with columnar epithelium. The appearance suggested atelectatic lung with epithelization of the alveoli. No evidence of bronchi could be made out, but the findings were consistent with what would be present in a lung cyst with chronic inflammation.

The patient showed some improvement with diffuse drainage, for a time, but the drainage continued. Transfusions were given because of the moderate anemia. Persistent drainage until the temperature is normal and evidences of infection have disappeared is contemplated, following which more radical surgical procedures will be undertaken. Roentgen examination after insertion of the tube showed reduction in the size of the cavities and diminution in the amount of fluid.

Comment: From a study of the films in Case 2, made by the local physician shortly after the onset of symptoms (Fig. 2A), it is evident that multiple pockets of fluid were present at the very beginning. The thin walls, the trabeculae within the cavities, the multiplicity of the cavities, and the lack of retraction of the lung, mediastinum, and diaphragm all support the diagnosis of lung cyst. The history of repeated rib resection and drainage without obliteration of the cavity is likewise suggestive. The demonstration of trabeculae of lung within the cavity at exploration and the biopsy findings confirmed the diagnosis of infected lung cysts and point the way toward radical surgery to be undertaken when conditions are more favorable. The failure of simple drainage over a period of a year and a half is characteristic.

In many respects this case suggests the syndrome of regional obstructive emphysema so well described by Caffey (4). The multiple pockets of fluid and gas occurring in an infant, presumably after an attack of pneumonia, are characteristic. But the persistence of the process with little change over a period of eighteen months, the development of a bronchial

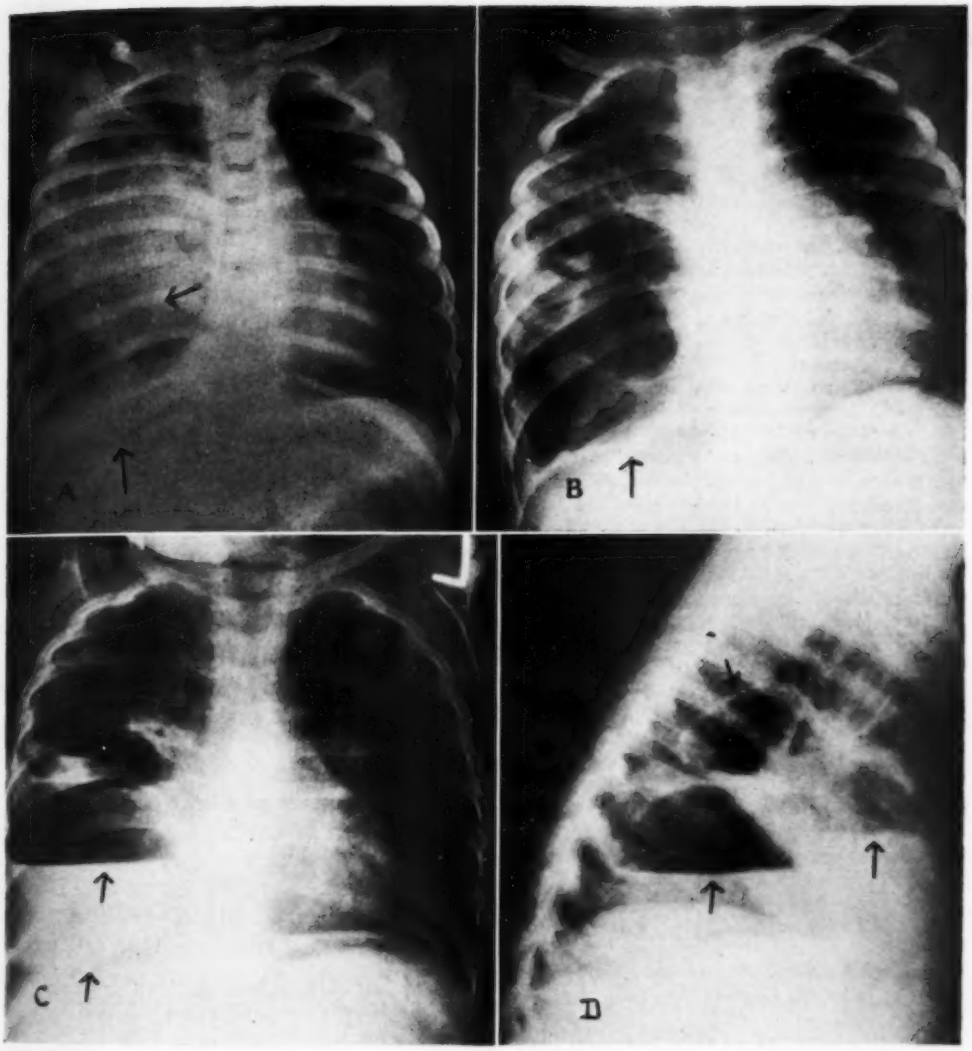


Fig. 2. Case 2: Multiloculated lung cyst with infection. A. Postero-anterior roentgenogram made Jan. 29, 1941, shortly after onset of symptoms, showing multiple pockets filled with fluid and gas. Note expansile character of cyst (arrow), just above diaphragm, and displacement of mediastinum.

B. Postero-anterior view 19 months later (Aug. 28, 1942). Sharply outlined, thin-walled, gas-filled pockets are shown. Note inferior margin (arrow).

C. Postero-anterior view (Sept. 1, 1942), upright position, showing fluid and gas levels (arrows). Note thin wall of cyst (upper arrow).

D. Lateral view (Sept. 1, 1942) showing multiple pockets with fluid and gas. Note fluid levels (arrows) and thin wall of upper cyst (arrow).

fistula with foul sputum, the enormous size attained by one of the pockets, and the fact that the fluid in the pockets predominated over the gas in amount, all indicate another type of process. Finally, the microscopic examination of excised tissue establishes the diagnosis of an infected cyst.[2]

A similar case, reported elsewhere (17), is here briefly reviewed.

CASE 3: H. H., a boy of 8 years, was first seen Sept. 30, 1930. He had been entirely well, apparently, until a year previously, when he had a cold followed by cough and expectoration. This had improved, but ever since that time he had had recurrent attacks of fever, cough, and expectoration. In May 1930 an attack of a similar kind was experienced. A rib resection was done for empyema; injection of the cavity then found demonstrated a bronchial fistula. The child entered the hospital with a diagnosis of bronchopleural fistula and encapsulated empyema in the left upper chest.

On x-ray examination there was found a very large, dense, rounded mass which, in the upright position, showed a small amount of gas at its upper surface, indicating communication with a bronchus. We, too, on examination at this time considered this to be an encapsulated empyema. This error in diagnosis was largely due to unfamiliarity with the syndrome of infected lung cysts.

Drainage of the cavity was accomplished on Oct. 3 by Doctor O. H. Wangensteen. Both gas and pus were obtained and a drainage tube was left in place. The cavity, however, persistently failed to close, and drainage continued over a period of years.

The patient was readmitted April 5, 1934, when he showed a large residual cavity. A catheter was introduced intercostally and suction was undertaken in order to re-expand the lung. There was a remarkable re-expansion during extreme suction, but the lung would collapse promptly when the suction was removed. The cavity was filled largely with air, and there was relatively little drainage of pus.

Some time after this we came to realize that this was really an infected lung cyst. The patient was again seen Oct. 10, 1938. The roentgenogram showed a large cavity in the left upper lobe almost entirely filled with air. A small amount of fluid was present at the base of the cyst.

The patient has had no further attacks of fever, cough, expectoration, or any other symptoms. He occasionally gets a little drainage, however, through a small opening which is still communicating with the external thorax. He refused further surgical procedures and apparently is getting along well.

Comment: This instance again illustrates the error of mistaking an infected lung cyst for an encapsulated empyema. The failure to obliterate the cavity, the continued drainage, and the alternate expansion and contraction of this large cavity should have indicated that this was a cyst rather than an empyema. Here, too, is well illustrated the possibility of a lung cyst becoming infected, producing symptoms, and then spontaneously, or after drainage, greatly improving. The fact remains that in this boy there is still a large cavity communicating both with a bronchus and with the outside, which may become infected again, with serious results. In all probability, extirpation of the cyst by lobectomy, as described by Churchill (6) and many other thoracic surgeons, would be the treatment of choice.

The evolution of a lung cyst from birth, through the process of fluid accumulation, bronchial communication, infection, and suppuration, is rarely observed. Hence, the following case, which has already been reported in part elsewhere (18), is detailed.

CASE 4: M. B., a boy, was born by spontaneous delivery in the University Hospital, Dec. 10, 1940, after a normal pregnancy. At birth the anus was not patent, but a small opening was finally discovered and dilated by catheters, following which meconium was readily passed. There was also cyanosis of intermittent character.

The physical findings were negative, but a roentgenogram of the chest made on the day of birth, because of cyanosis, revealed some density of the medial portion of the left lung and multiple rounded areas of rarefaction in the remainder of the same lung. The heart was displaced to the right (Fig. 3A). Within a few days the cysts expanded further until they filled most of the left hemithorax. Repeated roentgen examinations thereafter (Fig. 3B), until the child was four months of age, showed some

[2] Since the preparation of this paper further observations have been made on Case 2. Following the subsidence of the signs of infection, Dr. O. H. Wangensteen, on April 2, 1943, did a pneumonectomy, removing the right lung. It was found to contain three large cysts filled with somewhat turbid fluid and gas.

A photograph of a coronal section of the lung specimen is shown in Figure 7 (page 494). Comparison with Figure 3 indicates how faithfully the pathological anatomy was reproduced in the roentgenograms. The lobar divisions of the lung are almost completely absent. Note the three large cavities, the lining of which and the typical trabeculae are characteristic of congenital lung cyst.

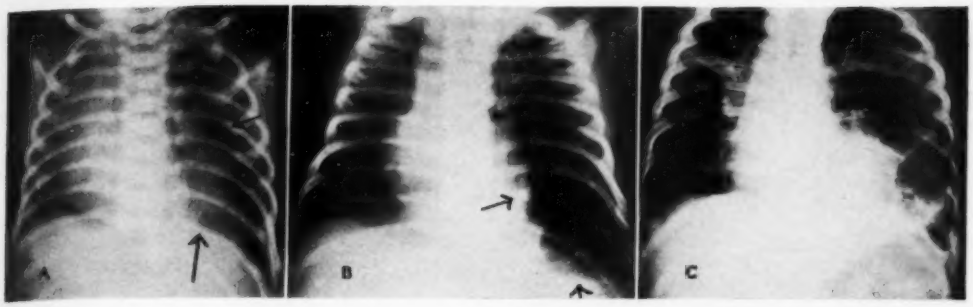


Fig. 3. Case 4: A. Postero-anterior view on day of birth (Dec. 10, 1940). Note density in medial portion of left lung and air-filled sacs in more lateral portion (arrow). The mediastinum is markedly displaced.
B. Postero-anterior view five weeks after birth (Jan. 15, 1941). Note large gas-filled pockets with thin trabeculae traversing the cysts. The mediastinum is still displaced.
C. Postero-anterior view one year later (Jan. 15, 1942). The pockets now show thicker walls and contain fluid and gas with extensive evidence of inflammation.

slight increase in expansion of the cysts, with further displacement of the heart to the right.

A mass was felt in the left upper quadrant, corresponding to the left kidney. Excretion urography showed the left kidney to be absent or non-functioning. The infant left the hospital Feb. 24, 1941, in good condition, without respiratory symptoms. He gained weight and developed normally.

On Jan. 8, 1942, the child became ill with cough, fever, and dyspnea. There was some discharge from the eyes, but no other signs. On entrance to the hospital on January 15, 1942, his temperature was 105°, pulse 150, and respirations 60. He had respiratory distress and an irritating cough. Breath sounds were suppressed on the left, there were rhonci, and, after coughing, medium moist râles in both lungs. The heart was shifted to the right. There was evidence of bilateral otitis media.

The leukocyte count was 35,600. The remaining laboratory findings were insignificant.

Roentgen examination (Fig. 3C) showed a striking change from the last examination, nine months before. The multiple cysts on the left showed thick walls with areas of atelectatic or consolidated lung between. Fluid was present in some of the cavities and there were many evidences of suppuration.

Re-examination, Feb. 3, 1942 (Fig. 4A and B), showed a considerable accumulation of fluid in the cysts. In the lateral view there was a rounded, massive, dense shadow projecting anteriorly and resembling somewhat an encapsulated empyema. This, obviously, represented one of the cysts, expanded and filled with fluid.

On Feb. 4, 1942, 40 c.c. of purulent fluid were removed from the cyst in the left lung. The culture was sterile. Roentgen examination (Fig. 4C) thereafter showed evacuation of one of the cysts with replacement of fluid by gas.

The temperature continued to fluctuate, but gradual improvement ensued, and the patient was discharged much improved on Feb. 11. His final x-ray examination indicated considerable evacuation of the cavities in the left lung, but some fluid still remained.

Comment: The congenital origin of this cyst is undisputed in view of the fact that it was demonstrable on the day of birth. This is not to say that it is hereditary or genetic in origin, as it may well have occurred as a result of some intrauterine process, but the important fact is that it was present at birth. It is interesting to note the presence of at least two other congenital anomalies.

The change from what appears to be a pure air cyst, into multiple pockets filled with fluid, obviously comes about as a result of a lining of bronchial mucous membrane present from the beginning but functioning only at a later period. Superimposed upon this is an infection. The effects of such a process are to produce pockets of purulent material in the lung. If it were not for the original films made at birth, the diagnosis of pneumonia with secondary abscesses or multiple pockets of empyema might well have been made. Here again the possibility of regional obstructive emphysema with cavitation (4) was considered. Attention is directed to the film reproduced in Fig. 4A which, taken by itself, with a history of infection, would most certainly have been thought to represent an encapsulated empyema.

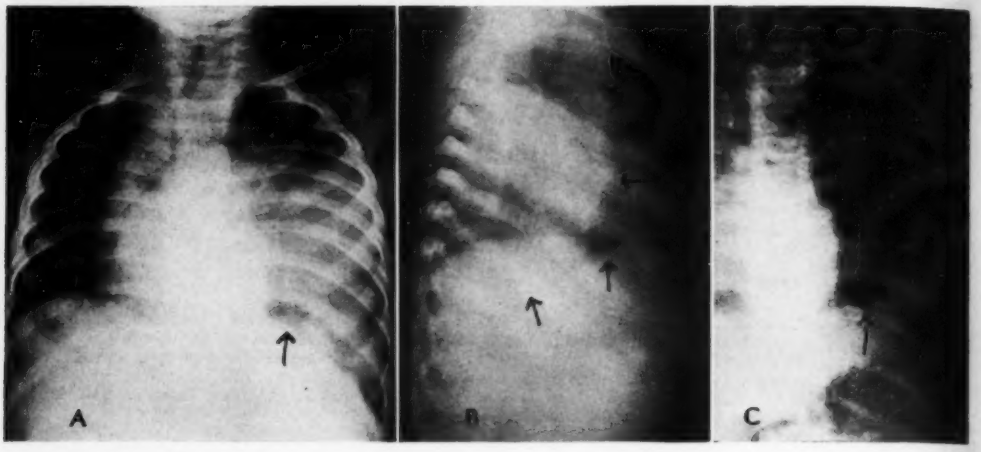


Fig. 4. Case 4: A. Postero-anterior roentgenogram made three weeks after Fig. 4C (Feb. 3, 1942). Note pockets largely filled with fluid except for one small cyst in the inferior portion containing only gas.
B. Lateral view same day (Feb. 3, 1942). Dense shadow of fluid-filled pocket, simulating closely encapsulated empyema, but extending below dome of diaphragm. Notice small cyst filled with gas only.
C. Postero-anterior view two days later (Feb. 5, 1942). Evacuation of pockets has occurred and they now contain chiefly gas.

It is important to observe, as Eloesser (10), Bruce (3), Maier and Haight (15), and others have shown, that a lung cyst, when infected, even if adequately drained, often does not clear up permanently, as does an empyema. Because of the lining with bronchial mucosa, secretion tends to continue in a lung cyst. Through the bronchial communication, a source of infection is present which will cause repeated attacks and produce a pocket of suppuration more or less permanently within the chest. Such lung cysts may not be amenable to the ordinary procedures, and it seems possible that some of the cases thought to represent recurrent chronic encapsulated empyema, which are resistant to drainage, may well be infected lung cysts rather than empyemas. Such a possibility was suggested by Maier and Haight (15), and our own experience tends to bear it out.

More radical surgery is necessary to prevent such a pocket from remaining as a permanent source of pulmonary suppuration and thus an ever-present danger to the host. It is possible to extirpate a lung cyst by means of segmental pneumonectomy, lobectomy, or even by total pneumonectomy if necessary, depending on the size and extent of the cyst under consideration, with a reasonable degree of safety. Other methods of treatment have been proposed, but, as Churchill (6) has pointed out, lobectomy is undoubtedly the method of choice.

The possibilities of early diagnosis of lung cyst by roentgen examination, confirmation by biopsy, and the splendid results achieved by lobectomy are well illustrated in the following case.

CASE 5: E. T., a male aged 16, presented himself first on Feb. 7, 1941, because of cough with purulent sputum. He gave a history of being entirely well until June 1940, when he experienced chills and fever. His fever continued and on July 13 physical examination indicated some evidence of fluid in the pleural cavity; aspiration showed it to be purulent. Rib resection was done July 15, 1940, and he made the usual recovery until July 30, when the temperature began to rise again. On July 31 a second rib was resected lower down and another large accumulation of purulent material was drained. Recovery was uneventful, but the patient continued to run a low-grade temperature from time to time and the cavity did not empty itself of fluid. In September he began to cough up foul-smelling sputum and the drainage from the area continued. Since that time he had raised large quantities of foul sputum. The leukocyte count was 9,100;

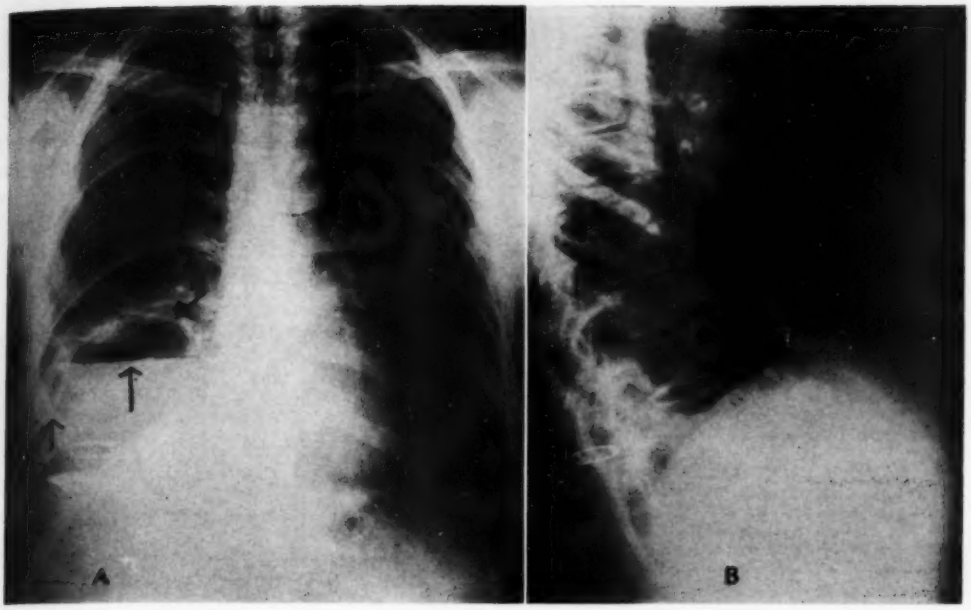


Fig. 5. Case 5: Infected cyst of lung simulating encapsulated empyema. A. Postero-anterior view (Feb. 8, 1941) showing pocket of fluid and gas with fluid level. Note thin wall of pocket (upper arrow), trabecula running through cyst (lower arrow), and defects in ribs. Iodized oil has been injected and can be seen at the bottom of the pocket. Metal markers are in position.

B. Lateral view (June 17, 1941) after prolonged drainage. Pocket is largely filled with gas and its very thin wall is well shown (arrows). Note trabeculae within cyst (arrow). Drainage tube is well shown.

there was a mild secondary anemia, but no other finding of significance. The temperature rose at one time to 100.8°, but was intermittent until drainage was done.

Films made by a local physician, in July 1940, at the time of the acute illness, were examined, but are not available for publication. These show a pocket of fluid in the right lung extending up to the 7th rib posteriorly, with a sharply defined clean-cut border. The first examination on entrance to the hospital, eight months later, shows a pocket of fluid and gas at the right base with a thin wall and some trabeculae within the pocket. The posterior portions of the 7th and 9th ribs show evidence of the old resections. The diaphragm is displaced downward. The lateral view showed the pocket to be far posterior. A drainage tube was seen in the cavity. Iodized oil was injected and indicated the lowest level of the cavity (Fig. 5A). A lateral view after evacuation of the fluid (Fig. 5B) brings out well the gas-filled pocket and the extremely thin wall. The absence of retraction, of thickening of the pleura elsewhere, the thin wall, and the trabeculae all led to the diagnosis of infected lung cyst.

On Feb. 8, 1941, a short segment of the eleventh rib was resected by Dr. John R. Paine. Much purulent material escaped, which on culture showed staphylococci. A segment of the wall was removed through the thoracoscope for biopsy, as this procedure was not undertaken at the time of drainage because of hemorrhage. Microscopic examination of the specimen by Dr. Robert Hebbel showed a pseudostratified columnar epithelium characteristic of a lung cyst. The temperature became normal, but the drainage continued.

The patient was readmitted on June 25, 1941, at which time the leukocyte count was 10,600 and the temperature ranged from 99.6 to 101°. Despite the evidences of infection, surgery was undertaken and the right lower lobe was resected by Dr. O. H. Wangensteen in the usual fashion. The patient made an uneventful recovery and is now entirely well.

The specimen was examined by Dr. Robert Hebbel. It weighed 300 gm. and consisted of a pyramidal mass with the apex corresponding to a drainage tube which passed into the infero-lateral border of the lobe. The greater portion of the mass was a single cystic cavity with a smooth, partly trabeculated wall. Microscopically the cyst was shown to be lined for the most part by pseudostratified columnar epithelium. In one area there was some squamous metaplasia. The subjacent tissue shows considerable scarring with irregular islands of pulmonary parenchyma and variable lymphocytic infiltration. The appearance was characteristic of a lung cyst with superimposed infection.

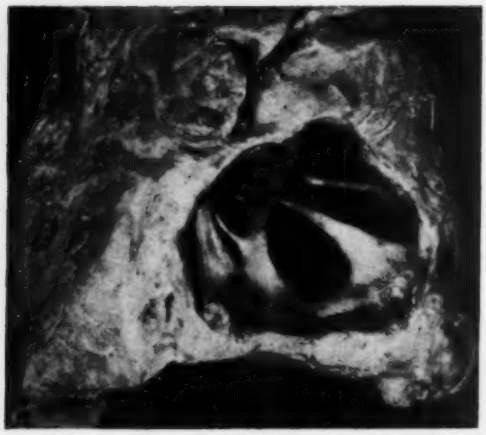


Fig. 6. Photograph of left lower lobe, removed by lobectomy, in a case previously reported. The cyst cavity with the atelectatic lung around it is well shown. In the cyst cavity can be seen numerous trabeculae which are so diagnostic of lung cyst. Such trabeculae can often be made out in the roentgenogram.

Comment: In this case, also, the roentgen findings suggested an infected lung cyst. The sharp outline, absence of thickened pleura, low position, lack of lung shrinkage, and very thin wall of the pocket are characteristic. The long history of repeated drainage without success was additional evidence. The biopsy specimen showed a typical microscopic picture.

The proper procedure in any such case is to drain the lung to the fullest extent possible and then do a resection of the lobe or, if possible, of the cyst itself. The prompt and complete cure is gratifying and is typical of the result which may be achieved.

We have observed two other cases previously reported (17), one of which was almost identical and the other similar to the case reported above. In both instances the result of lobectomy was a complete cure.

DISCUSSION

From the point of view of the roentgenologist the important feature is to determine what are the findings which should lead to a suspicion of lung cyst and arouse sufficient interest to stimulate the surgeon to further study and removal of a specimen from the wall of the pocket for biopsy. Some of these findings have been detailed above in connection with the case reports. Most important is the sharply encapsulated, well defined pocket standing out separately from the remainder of the chest, the absence of associated pleural thickening throughout the hemithorax, the frequently very low position of the pocket, the absence of any retraction of the mediastinum or diaphragm toward the encapsulated pocket, and the demonstration of a relatively thin wall when air replaces the fluid within the pocket itself. Another important finding is the demonstration of trabeculae within the cyst, representing strands of lung tissue. Such trabeculae can be felt by the surgeon when exploring a lung cyst. Figure 6 is a photograph of the specimen from one of

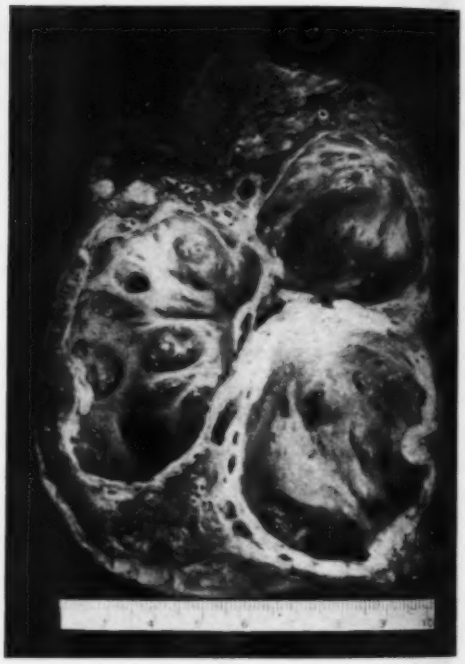


Fig. 7. Case 2: Coronal section of lung specimen, showing absence of lobar divisions and presence of three large cavities with typical lining and trabeculae. See footnote on page 490 and compare with Fig. 3, p. 491.

our cases (previously reported) and demonstrates very well the nature of the trabeculae. If, added to any of these considerations, there is a history of repeated lung infections or repeated drainage procedures, the stimulation to do a biopsy is greatly enhanced.

Attention should again be directed to the descriptions of regional obstructive emphysema by Caffey (4), interstitial emphysema by Peirce and Dirkse (16) and to a putrid pulmonary necrosis by Kessel (12) and others. These conditions, as well as those mentioned above, must be differentiated. Maier (14) has recently reviewed the differential diagnosis most adequately.

The result of the biopsy examination may not necessarily be unequivocal. If pseudostratified columnar epithelium is demonstrated, it usually indicates a lung cyst. It is, of course, possible for bronchial epithelium to grow through a fistula into an abscess and by metaplasia produce an epithelial lining. The fact that this occurs, however, is not of any great importance, because once this process has taken place the pocket, even though it originated as a lung abscess, is for all practical purposes a cyst. It has a secreting lining which will tend to keep it from collapsing under drainage. The demonstration of endothelium or of a simple inflammatory membrane will lend strong credence to the opinion that the process is not a lung cyst, but rather a simple abscess or encapsulated empyema. The biopsy is not difficult to do at the time of drainage, which in itself is usually indicated in any event, as no radical surgical procedure can be attempted before the purulent cavity has been thoroughly evacuated.

The importance of observation of such cases cannot be exaggerated. We have now seen 6 such cases in which the patient was subjected to repeated attacks of pulmonary suppuration, which endangered his life on each occasion and more or less completely disabled him. A radical surgical procedure has resulted in a cure in 4 of these cases. In the remaining 2 it has not yet been applied because of the age of the patients and their general condition. Under reasonably favorable conditions, it is possible to apply this with relatively little risk.

SUMMARY AND CONCLUSIONS

The infected cyst of the lung as a source of pulmonary suppuration is described.

Cases are reported to illustrate:

(1) The development of a bronchial fistula in a fluid-filled cyst.

(2) Multiple infected cysts of the lung simulating loculated empyema or lung abscess.

(3) A single large cyst of the lung mistakenly diagnosed encapsulated empyema. Repeated rib resections with drainage failed to cure the patient.

(4) The eventual development of gas-containing lung cysts observed at birth into multiple pus-containing pockets simulating lung abscesses.

(5) A single infected cyst of the lung mistakenly diagnosed as encapsulated empyema, failing to clear up after several rib resections. The correct diagnosis was made by roentgen examination, confirmed by biopsy, and the patient was cured by lobectomy.

The roentgen findings which differentiate infected lung cyst from other lesions are detailed.

Biopsy of the wall at the time of drainage is the best means of diagnosis.

Radical surgery—extirpation of the portion of the lung containing the cyst, preferably lobectomy—is the best method for attaining a permanent cure.

In cases with a suppurative cavity in the chest, especially in those which do not respond to drainage, the diagnosis of infected lung cyst should be considered.

University Hospital
Minneapolis, Minn.

BIBLIOGRAPHY

1. ADAMS, W. E., AND SWANSON, W. W.: Internat. Clin. 4: 205–220, December 1935.
2. ANSPACH, W. E., AND WOLMAN, I. J.: Surg., Gynec. & Obst. 56: 635–645, March 1933.
3. BRUCE, T.: Acta med. Scandinav. 102: 295–323, 1939.

4. CAFFEY, J.: Am. J. Dis. Child. **60:** 586–605, September 1940.
5. CHENEY, G., AND GARLAND, L. H.: Am. J. M. Sc. **196:** 699–703, November 1938.
6. CHURCHILL, E. D.: J. Thoracic Surg. **6:** 286–311, February 1937.
7. DIAMOND, S., AND DURHAM, W. R.: Am. Rev. Tuberc. **41:** 719–731, June 1940.
8. DUBROW, J. L.: Radiology **24:** 480–488, April 1935.
9. DUBROW, J. L., AND WYNN, W. R.: Am. Rev. Tuberc. **38:** 262–265, August 1938.
10. ELOESSER, L.: Radiology **17:** 912–929, November 1931.
11. FREEDMAN, E.: Am. J. Roentgenol. **35:** 44–52, January 1936.
12. KESSEL, L.: Arch. Int. Med. **45:** 401–411, March 1930.
13. KOONTZ, A. R.: Bull. Johns Hopkins Hosp. **37:** 340–361, November 1925.
14. MAIER, H. C.: Am. J. Surg. **54:** 68–81, October 1941.
15. MAIER, H. C., AND HAIGHT, C.: J. Thoracic Surg. **9:** 471–494, June 1940.
16. PEIRCE, C. B., AND DIRKSE, R.: Radiology **28:** 651, 1937.
17. RIGLER, L. G.: Internat. Clin. **4:** 203–221, December 1941.
18. RIGLER, L. G.: Journal-Lancet **62:** 195–198, May 1942.
19. SANTE, L. R.: Radiology **33:** 152–165, August 1939.
20. SCHENCK, S. G.: Am. J. Roentgenol. **35:** 604–629, May 1936.
21. SCHENCK, S. G.: Arch. Int. Med. **60:** 1–21, July 1937.
22. SELLORS, T. H.: Proc. Roy. Soc. Med. **33:** 337, April 1940.
23. SELLORS, T. H.: Tubercle, **20:** 49, November 1938.
24. SHARPE, C. T.: Radiology **34:** 692–697, June 1940.
25. SWANSON, W. W., PLATOU, E. S., AND SADLER, W.: Am. J. Dis. Child. **35:** 1024–1031, June 1928.
26. WEAVER, R. G., AND VON HAAM, E.: Surgery **4:** 917–929, December 1938.
27. WOOD, W. B.: Proc. Roy. Soc. Med. **33:** 335, April 1940.

DISCUSSION

Fred J. Hodges, M.D. (Ann Arbor, Michigan): There are three commonly employed methods of opening the discussion of a scientific paper. One of these is to indulge in flowery compliments; another to bring to the meeting a box of lantern slides with which to illustrate a supplementary paper, and a third is to disagree violently with the original speaker. None of these methods seems appropriate to the present occasion.

The program committee has shown farsightedness in withholding Doctor Rigler's paper until the end of a long, busy day, and Doctor Rigler has not disappointed those of us who have stayed through until the end. The opening discussion might well be limited to praise of his article in more detail than the recitation of empty compliments.

I am sure that Doctor Rigler did not intend to warn us that lobectomy or major surgery is required in the treatment of all lesions that appear in chest roentgenograms as empty, spherical areas within the lung. The great majority of such lesions do not fall in the category he has described. Two words, well established in medical terminology, "bulla" and "bleb," are for some reason seldom employed by roentgenologists. The lesions they represent are certainly quite common and very frequently occur after inflammatory disease of the lung, developing more or less accidentally as the result of local disturbance of intimate lung structure. In most instances they will disappear if strictly left alone. Bronchiectasis of the cystic type, when examined after removal of part of the lung, is clearly recognizable as such. This condition is seldom responsible for the complications which Doctor Rigler has been describing. He has presented in splendid fashion the material on which his conclusions are drawn, beginning with uncomplicated cystic lesions and leading up to the confusing group which stimulated his paper. You will remember one of his slides which best exemplifies the fact that not every situation which at first seems to be empyema actually represents the accumulation of purulent fluid in the pleural space. The small, spherical lesion thrown into relief following pneumothorax was actually beneath the visceral pleura. As he has pointed out, one must suspect the presence of a pulmonary cyst which has become infected when dealing with situations which appear to be empyema. It is seldom that one has access to earlier roentgenograms in which the diagnosis is clear cut.

It happens that Maier and Haight did their work in our hospital and that I am somewhat familiar with their material. They were stimulated to write about infected pulmonary cysts because of mistakes which they had made, with the full collaboration of our department, in misjudging encapsulated empyema and by biopsy findings which brought these errors to light. The discovery of cyst-wall fragments in biopsy specimens, showing definitely the characteristic epithelial lining, made it obvious that they were not dealing with ordinary empyema.

In one of Doctor Rigler's slides the trabeculae which frequently traverse pulmonary cysts were beautifully shown.

Roentgen Diagnosis of Placenta Praevia[1]

GEORGE I. BAYLIN, M.D., and SAMUEL S. LAMBETH, M.D.

Department of Roentgenology and Department of Obstetrics and Gynecology, Duke University Hospital, Durham, N. C.

VAGINAL BLEEDING in the last trimester of pregnancy is quite common, and even though it is frequently of little consequence, the physician in attendance must always consider the possibility of placenta praevia as the underlying cause.

The incidence of placenta praevia varies considerably with the type of practice. Whereas, in general practice, it is no more frequent than one case in every 300 births (1, 2), Stander (3) found that it occurs once in every 180 hospital deliveries.

The usual method of determining the placental position has been the performance of a thorough pelvic examination. The obvious disadvantages of this procedure are too well known to be expounded here. Placenta praevia carries a high mortality rate and, since pelvic examination contributes distinctly to this rate, any diagnostic procedure that eliminates its performance deserves serious consideration.

In 1934, Snow (4) suggested the use of soft-tissue roentgenography in order to demonstrate the position of the placenta. Several other authors (6, 8, 10, 11) have since contributed favorable reports. Snow (5) summarized the work on this problem in 1939 and showed conclusively that the method is practical, reliable, and simple. Dippel and Brown (8) reported 11 cases of placenta praevia in which the diagnosis was made correctly by x-ray visualization. These authors state that this method has greatly reduced the number of pelvic examinations prior to delivery.

Snow (9) routinely takes three films of all late pregnancy cases, the conventional anterior-posterior and lateral films plus a soft-tissue lateral film. He injects 200 c.c. of air into the bladder in order to afford greater contrast between the placenta and the surrounding pelvic tissues. It is interesting to note that by adherence to this simple routine, he has discovered several cases of placenta praevia before the development of any symptoms.

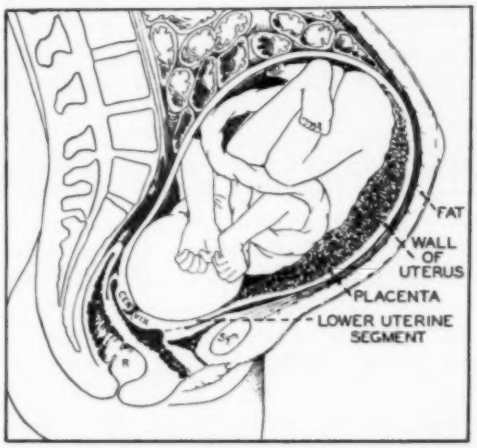


Fig. 1. Sketch showing important anatomical structures outlined in soft-tissue roentgenograms. Modified after Williams: Textbook of Obstetrics.

The actual technic for taking lateral soft-tissue films is not difficult, nor does it require any elaborate equipment. We have found that a low kilovoltage with relatively short exposure time results in films of sufficient contrast to render the various anatomical structures visible. The use of a plastic filter to prevent over-penetration of the anterior abdominal soft tissues has proved effective in our hands and has, likewise, eliminated the necessity of taking separate films for the posterior and anterior structures. The uterine wall and the maternal abdominal wall are easily seen, and since the placenta usually occupies 20 to 30 per cent of the endometrial surface, it also is readily identified. The placenta is most often implanted on the anterior or posterior wall of the fundus

[1] Accepted for publication in October 1942.

(Figs. 1–3), and is revealed as a thickened soft-tissue shadow fused with the uterine wall. Frequently, the indentations in the placenta produced by pressure from fetal soft parts (Fig. 7) are clearly seen. The zones of decreased density between the fetus and uterine wall have been shown to be due to subcutaneous fetal fat.

A thorough knowledge of the normal structures is essential to accurate x-ray diagnosis. Whenever the placental shadow cannot be demonstrated at the usual sites, a low implantation exists. Several observers have stated that low anterior attachments occur much more frequently than low posterior ones, in the ratio of eight to one. Although we have not observed so high an incidence of low anterior attachments, the principle has been found to be true. It is important to bear in mind the ratio of the size of the placenta to the extent of the uterine wall, so that a proper evaluation of the proximity of the placenta to the cervical os can be made; otherwise, errors will ensue when a placenta praevia marginalis is present. Low posterior implantations are more difficult to diagnose, chiefly because the x-rays must penetrate a greater thickness of tissue and, as a result, contrast is sacrificed. One point which has aided us in these cases has been an increase in the distance between the sacrum and fetal head because of the interposition of the thick placenta (Figs. 3 and 4).

Certain factors interfere with satisfactory results and some observers (15, 16, 17) have therefore been inclined to discredit the value of soft-tissue studies. According to Brown and Dippel (11), obesity interferes with accurate placental visualization, but in our experience this has not proved true. The chief causes of inaccurate visualization have been hydramnios multiple pregnancies, breech presentations, and poor films. In some instances, a supposedly poor film, when viewed under a bright or different colored light, reveals enough detail for a definite diagnosis.

Air in the bladder has proved a help according to one observer (7), but it is not essential. Indeed, a cystogram in the anteroposterior view may prove misleading. A separation of the bladder from the fetal head on this type of film led to a serious error in one of our cases (Fig. 5) before we had instituted routine soft-tissue studies. Ude and Urner (18), however, reported the successful use of iodide cystograms in the roentgenologic demonstration of placenta praevia. They felt that the lateral film was not necessary, but subsequent experience has proved the great value of the lateral soft-tissue film. Moreover, incorporating the cystogram with a soft-tissue roentgenogram will greatly enhance the contrast.

Certain widely used textbooks of obstetrics (12, 13, 14) fail to stress or in some instances even to mention the use of soft-tissue films in the diagnosis of placenta praevia. Our experience at Duke Hospital has been so encouraging that we feel this mode of diagnosis deserves wider recognition than it is now accorded. During the past eighteen months, many soft-tissue films have been obtained in cases of bleeding in late pregnancy and early labor. Sixteen patients ultimately proved to have placenta praevia, at the time of vaginal delivery or cesarean section. Only those cases in which the placenta covered the cervical os or was palpated within 2 cm. of the os were called placenta praevia, and only such cases are included in our series. In all of our cases, the exact site of the placenta was verified at the time of vaginal or abdominal delivery.

As a result of careful evaluation of the x-ray appearances and the actual findings at delivery, we believe that definite evidence has accrued attesting the value of roentgenograms in placental diagnosis. Of 16 cases considered, the x-ray diagnosis was proved correct in 14. We were able to state the location of the placenta in all the cases. Moreover, in 3 instances the diagnosis of complete placenta praevia was made (Fig. 6), demonstrating that this condition can be differentiated from the marginal type (Fig. 7). This differentiation has proved most helpful to the physicians in the handling of these cases.

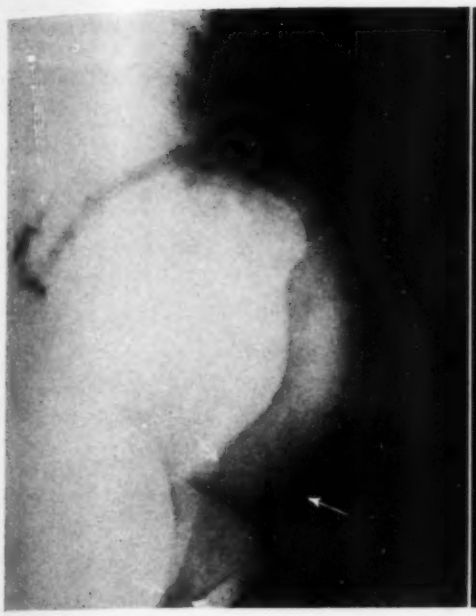


Fig. 2. Normal anterior implantation of placenta. Arrows show increased thickness of soft-tissue shadow at placental site. The subcutaneous fat and the muscle layer of the abdominal wall are easily seen. Retouched.

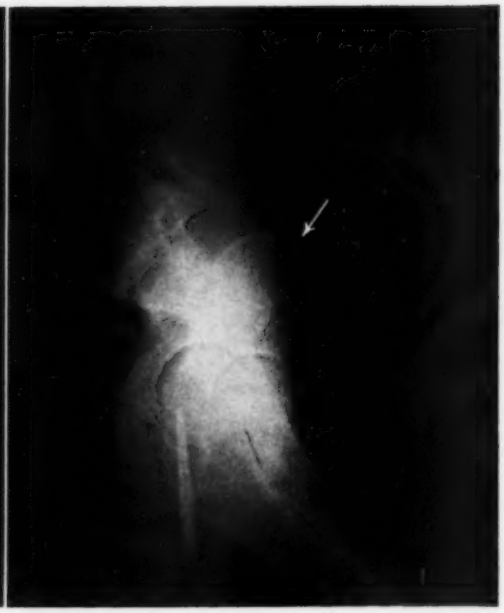


Fig. 3. Tip of Halsted clamp shows approximate site of cervix in relation to sacral promontory and symphysis pubis. Arrow shows the normal relationship of the floating fetal head to the sacral promontory.

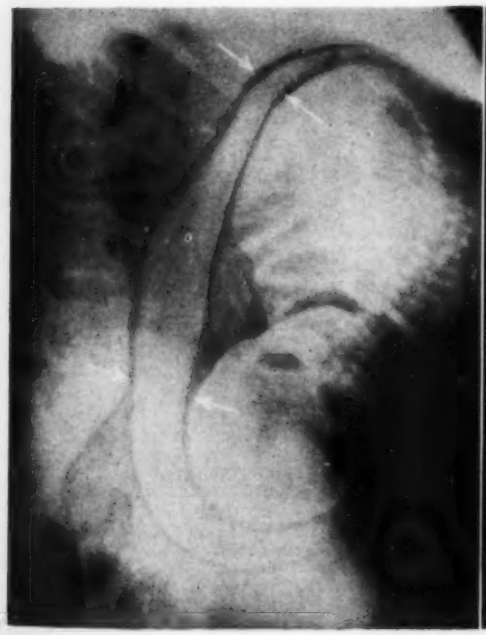


Fig. 4. Posterior implantation in placenta praevia. The greater distance of the fetal head from sacral promontory than in Fig. 3 may be observed. Retouched.

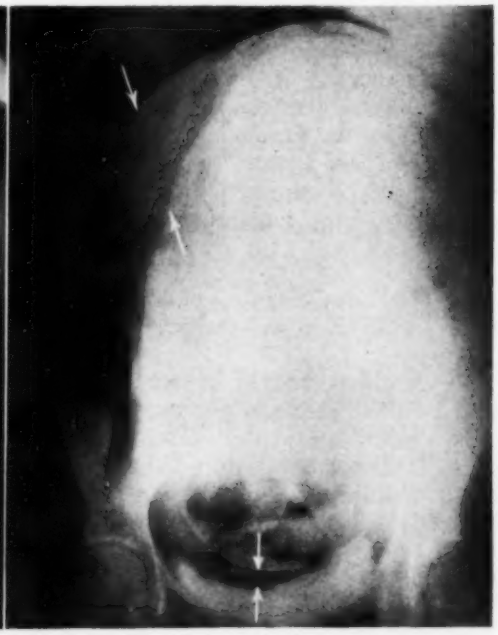


Fig. 5. Cystogram made with an opaque iodide solution in the bladder, in attempt to locate placenta. Arrows at top of picture show actual placental location. Retouched.

Fig. 6. Complete placenta praevia. Arrows show difference in thickness of soft-tissue shadow representing uterine wall and uterine wall plus placenta. Retouched.

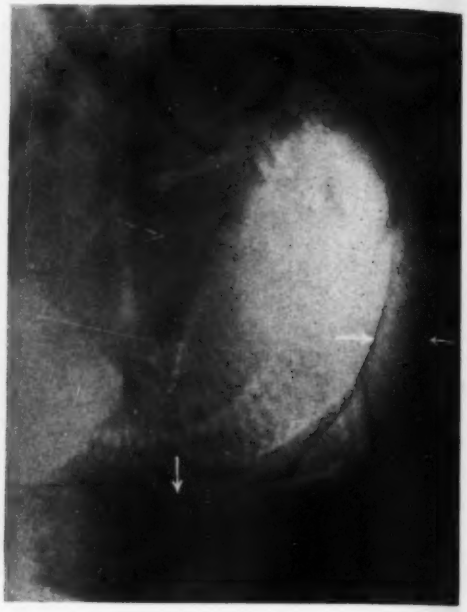


Fig. 7. Placenta praevia marginalis. Indentation of placenta by fetal soft parts may be observed. Retouched.

Of the two "inaccurate" cases, one was diagnosed as an anterior attachment, without any mention of the fact that the placenta descended to the cervical os. Lack of detail on the film was responsible. In the second "inaccurate" case, the film was not properly interpreted, and later analysis revealed a low implantation.

CONCLUSIONS

1. The x-ray diagnosis of abnormal placental attachment was correct in 14 out of 16 cases.
2. A differentiation between marginal and complete placenta praevia was made.
3. Soft-tissue demonstration of the placenta is simple, safe, and reliable, and the method deserves more widespread use in obstetrical diagnosis.

NOTE: In order to show on the printed page as much as possible of the detail which can be observed on the film, it was necessary to retouch the roentgenograms used in this article. For this excellent work, we express appreciation to the Departments of Illustration and Photography at Duke Hospital.

Duke University Hospital
Durham, N. C.

BIBLIOGRAPHY

1. KIMBROUGH, R. A.: Mississippi Doctor **18:** 557–565, March 1941.
2. HOLMES, R. W.: Am. J. Surg. **48:** 61–100, April 1940.
3. STANDER, H. J.: in Williams' Obstetrics, 8th ed., 1941.
4. SNOW, W., AND POWELL, C. B. Am. J. Roentgenol. **31:** 37–40, January, 1934.
5. SNOW, W., AND ROSENSOHN, M.: Am. J. Roentgenol. **42:** 709–717, November 1939.
6. JARCHO, J.: Am. J. Surg. **48:** 485–522, May 1940.
7. PRENTISS, R. J., AND TUCKER, W. W.: Am. J. Obst. & Gynec. **37:** 777–787, May 1939.
8. DIPPEL, A. L., AND BROWN, W. H.: Am. J. Obst. & Gynec. **40:** 986–994, December 1940.
9. SNOW, W.: Personal communication, December 1941.
10. DIPPEL, A. L., AND BROWN, W. H.: New England J. Med. **223:** 316–323, Aug. 29, 1940.
11. BROWN, W. H., AND DIPPEL, A. L.: Bull. Johns Hopkins Hosp. **66:** 90–105, February 1940.
12. DELEE, J. B.: Principles and Practice of Obstetrics, 7th ed., 1940.
13. TITUS, PAUL: Management of Obstetric Difficulties, St. Louis, C. V. Mosby Co., 2d ed., 1940.
14. BECK, ALFRED: Obstetrical Practice, 2d ed., 1940.
15. DAVIS, M. E.: Internat. Abstr. Surg. **68:** 504–512, 1939, in Surg., Gynec., & Obst., May 1939.
16. BOWEN, G. L.: M. Clin. North America **25:** 649–657, May 1941.
17. CARVALHO, M. A.: Am. J. Obst. & Gynec. **39:** 306–312, February 1940.
18. UDE, W. H., AND URNER, J. A.: Am. J. Obst. & Gynec. **29:** 667–679, May 1935.

Polyostotic Fibrous Dysplasia: Review of the Literature with Two Additional Cases[1]

NATHAN JAMES FURST, M.D., and ROBERT SHAPIRO, M.D.
Newark, N. J.

HISTORY

EVER SINCE THE publication of von Recklinghausen's (91) monograph in 1882, the literature on fibrocystic disease of bone has become increasingly abundant and confusing. In retrospect, it is obvious that von Recklinghausen described not one disease but a number of heterogeneous, unrelated pathologic conditions which had, as a common denominator, the production of fibrocystic-like bone changes. For many years, his name has been associated with hyperparathyroidism and neurofibromatosis. As a matter of fact, it is not unlikely that some of his original cases may have been examples of polyostotic fibrous dysplasia.

The latter disease entity was first popularized in this country by Albright and his co-workers in 1937 (3) and by Lichtenstein in 1938 (50). It had been known on the continent for some time prior to its recognition here. In 1922, Wieland (98) in Germany wrote an article entitled *Osteitis Fibrosa Cystica Congenita*, which may well have been a discussion of polyostotic fibrous dysplasia. The same year, Weil (94) reported a classical case of polyostotic fibrous dysplasia under the title *Precocious Puberty and Bone Brittleness*.

Weiss (95), in 1923, published a paper on the unilateral variety of multiple chondromata, which probably referred to polyostotic fibrous dysplasia. In 1929, Winter (99) presented a case of generalized osteitis fibrosa cystica in the absence of a parathyroid tumor. The same year, Ivimey (42), for the first time in the American literature, described a typical case under the title *Bone Dystrophy with Characteristics of Leontiasis Ossium, Osteitis Deformans, and Osteitis Fibrosa Cystica in a Child*.

Two years later, in 1931, Telford (83) in England published the first gross and microscopic description of the pathologic nature of the disease. At the same time, Hunter and Turnbull (40), in their article on hyperparathyroidism, listed one case which was probably polyostotic fibrous dysplasia.

The following year, Leader and Grand (49), Gaupp (30), Priesel and Wagner (68), Freedman (25), and Braid (9) also reported isolated cases of polyostotic fibrous dysplasia. In 1933, Snapper and Parisel (77) described a case of polyostotic fibrous dysplasia under the title *Xanthomatosis Generalisata Ossium*. During the same year, Rypins (73), Fairbank (22), Salzer (74), and Stalmann (79) contributed additional examples to the literature.

In 1934, Goldhamer (31), and Freund (26) wrote papers describing this disease under the name of *osteodystrophia fibrosa unilateralis*, while Borak and Doll (7) reported a case which they termed *unilateral von Recklinghausen's disease of bone and precocious puberty*. Hummel (39) described three cases as *juvenile Paget's disease*.

The following year, Elmslie (21) discussed generalized osteitis fibrosa cystica not due to hyperparathyroidism, and in 1936, Freund and Meffert (27) enumerated the various forms of non-generalized fibrous osteodystrophy.

In spite of these individual reports, the significance of polyostotic fibrous dysplasia was not fully appreciated in this country until Albright and Lichtenstein, working independently, published their observations in 1937 and 1938. Since that time, numerous case reports have found

[1] From the Department of Roentgenology, Newark Beth Israel Hospital, Newark, N. J. Accepted for publication in December 1942.

their way into the literature, and a more widespread recognition of the disease has been achieved.

ETIOLOGY

As yet, the exact etiology of polyostotic fibrous dysplasia has not been definitely established, although several theories have been advanced in an effort to explain the bizarre clinical and radiographic findings characteristic of the disease.

(*1*) *Atypical Ollier's Disease* (*Achondroplasia, Skeletal Enchondromatosis*): Freund (26) suggested that polyostotic fibrous dysplasia might be an unusual form of Ollier's disease, and cited Bentzon's (6) experimental work in support of his theory. The latter investigator, by injecting absolute alcohol into rabbits in an effort to influence the sympathetic cord, was able to produce changes in the bones resembling those found in Ollier's disease. Freund believed the fibrous changes in the bones of his patient to be similar to those found in Bentzon's animals and concluded that they were a reaction to active hyperemia of the bone tissue. He further ascribed the hyperemia to anomalies in the vegetative nervous system resulting in paresis of the muscular coat of the blood vessels and vascular dilatation.

This theory fails to explain the pigmentation, the endocrine dysfunction, and precocious puberty associated with polyostotic fibrous dysplasia. Furthermore, Bentzon's experimental results were inconstant, the bone changes being present in only one animal. In addition, the histologic picture of the involved bone in the two diseases is quite dissimilar.

(*2*) *Primary Hepatic Disease:* Because of the coexistence of icterus neonatorum in some of the cases of polyostotic fibrous dysplasia, Braid (8, 9) proposed the hypothesis that a function of the liver concerned with the storage and utilization of vitamins had been damaged, resulting in a disturbance of bone growth. In support of this hypothesis, he cited the experimental work of Buchbinder and Kern (12–14). The latter investigators were able to demonstrate radiologic changes in the bones of puppies, after tying off the common duct and producing chronic jaundice. These changes consisted in cortical thinning, with relatively wide medullary spaces, a marked degree of osseous rarefaction, and, in one animal, actual cysts. In addition, the disturbance produced by thyroparathyroidectomy in these animals was considerably less severe than in normal dogs, and tetany did not appear even when the serum calcium reached the tetany level. To Braid, these findings indicated that the altered calcium metabolism in obstructive jaundice was due to another factor, in addition to the absence of bile from the intestine. He thought it likely that the liver played a role in the metabolism of calcium, and also in normal growth of bone and nervous tissue.

Braid's hypothesis, however, does not elucidate the cause of the endocrine abnormalities, the pigmentation, and the fibrocystic character of the bone changes in polyostotic fibrous dysplasia. Furthermore, since the serum calcium in polyostotic fibrous dysplasia is usually within normal limits, the jaundice could not explain the osseous lesions. Finally, the difference in the radiologic pictures found in these two conditions tends to militate against the acceptance of the hypothesis.

(*3*) *Abnormality of the Bone-Forming Mesenchyme:* Lichtenstein (50) believes the primary defect in polyostotic fibrous dysplasia to be a disturbance in the function or development of the bone-forming mesenchyme. This abnormality supposedly results in a replacement of the substantia spongiosa and a filling in of the medullary cavity by fibrous tissue in which primitive, poorly calcified new bone trabeculae are developed by osseous metaplasia.

This concept may offer an explanation of the character of the bone lesions, but fails to account for the tendency to unilaterality of the disease, the pigmentation, and the endocrine dysfunction.

(4) *Primary Neurologic or Embryologic Defect:* Albright (3, 4) feels that the tendency toward unilaterality of the bone and

cutaneous lesions precludes any primary endocrine or metabolic disorder as their cause. He suggests the possibility of a neurologic or embryologic defect, *e.g.*, a neurologic lesion disturbing the afferent impulses to the anterior lobe of the pituitary gland.

There is some evidence, both clinical and experimental, which tends to substantiate Albright's hypothesis. The ability of the gonadotropic hormone of the anterior lobe of the pituitary gland to produce precocious sexual development in the experimental animal has been well established. In human females with polyostotic fibrous dysplasia, increased secretion of this hormone might perhaps account for the early appearance of the menses and the rapid development of the secondary sex characteristics.

Too, the relationship of the anterior lobe and the pars intermedia to pigmentation is well known. Acromegaly, for example, is not infrequently associated with brownish pigmentation resembling large freckles on the face, neck, upper chest, and arms. Also, it has been repeatedly demonstrated that extirpation of the pituitary gland in tadpoles results in their growth into albino frogs. Conversely, injection of pituitary extracts into frogs darkens the color of their skin. Thus, a connection between the pituitary gland and the pigmentation of the skin in polyostotic fibrous dysplasia is not wanting.

It is not impossible that some as yet undetermined disturbance of the parathyrotropic hormone of the anterior pituitary might account for the fibrocystic-like changes of the bones in polyostotic fibrous dysplasia. At one time, one of us (R. S.) thought that the ionizable serum calcium fraction in polyostotic fibrous dysplasia might be low, thus explaining the bone lesions in the face of a normal total serum calcium. This would mean that a greater portion of the serum calcium was present in the inactive form, *i.e.*, bound with protein. Chemical investigation, however, has failed to substantiate this belief.

The hypothalamic control of anterior pituitary function has been recognized for some time, as a result of numerous animal experiments (28). In addition, Ford and Guild (23) have called attention to the relation of various hypothalamic lesions to the development of precocious puberty. They mention two cases in which measles encephalitis was followed by precocious puberty in girls, and one instance of precocious puberty in a boy as a sequel of epidemic encephalitis. They concluded, after a survey of the literature, that destructive lesions in the region of the third ventricle could produce the syndrome of macrogenitosomia praecox.

Shellard (75) reported a case of polyostotic fibrous dysplasia in a female in whom pigmentation was first noted after an attack of poliomyelitis at the age of eighteen months. The patient later showed precocious puberty and typical bone lesions. Tobler (85) published a similar case in a girl of six and a half years who had poliomyelitis at the age of three, followed by "the grippe" a year later, and the appearance of characteristic osseous lesions. Heard, Schumacher and Gordon (34) described a case of polyostotic fibrous dysplasia in a three-year-old boy, associated with diabetes insipidus. At the age of twenty-one months, the child had suffered a cranial injury, following which the disease developed. Vickers (88) also reported precocious sex development at the age of eight months in a male child in whom a tumor of the third ventricle was found at operation.

It is not inconceivable, therefore, that the sequence of events in polyostotic fibrous dysplasia is somewhat as follows: some hypothalamic lesion in the region of the third ventricle produces secondary disturbances in the anterior lobe of the pituitary, resulting in abnormal stimulation of its various component tropic hormones. This hypothesis, in addition to explaining the usual findings in polyostotic fibrous dysplasia, would also account for the occasional occurrence of concomitant hyperthyroidism in some cases.

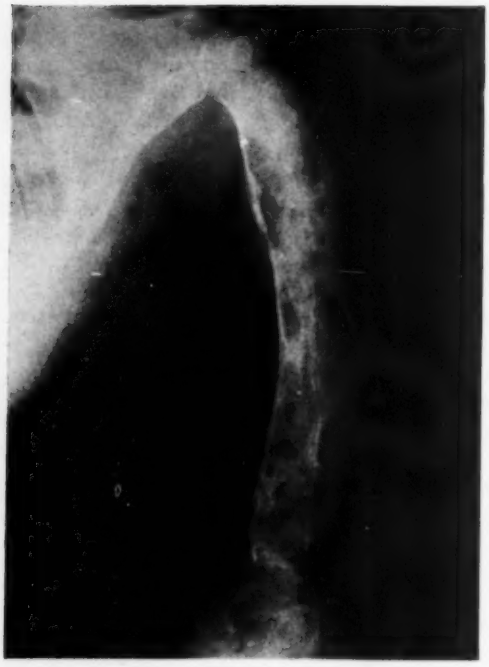


Fig. 1. Case 2: Left humerus, showing fibrocystic-like lesions. This film, taken five weeks after Fig. 5, also illustrates union of the pathological fracture of the humerus.

(5) *Multiple Embryonic Defects:* Neller (63) is of the opinion that polyostotic fibrous dysplasia is due to embryonic defects involving multiple systems. He believes that the various component signs and symptoms of polyostotic fibrous dysplasia occur individually more frequently than they do simultaneously, and that this militates against a defect in a single system.

It is worthy of note, in this respect, that Stauffer (80) reported a case of polyostotic fibrous dysplasia associated with multiple vascular aneurysms. Similarly, Coleman (15) described a case in a thirteen-year-old boy with partial coarctation of the aorta, an aneurysm of the beginning of the thoracic aorta, and an atrophic right kidney. Such cases, however, are rare, and this hypothesis would hardly seem to explain the constant occurrence of the classical findings in the vast majority of patients with polyostotic fibrous dysplasia.

SIGNS AND SYMPTOMS

The patients are usually children or young adults in whom the disease has been present for some time before medical aid is sought. Frequently, the chief complaint is a limp, pain or deformity of one of the lower extremities (pain in the hip or tibia, coxa vara, bowing of the femora, etc.), or deformity and pain in one of the upper limbs. On the other hand, attention may first be drawn to the presence of the condition as a result of a pathological fracture. Occasionally, the first external manifestation of the disease is facial asymmetry and ocular proptosis, due to involvement of the skull. Neller (63) reported one case in which the patient was operated on for a supposedly infected cyst of the scalp. This eventually proved to be a protrusion of the meninges through the bone defect in the skull produced by the fibrous involvement of the latter.

In addition, these patients frequently have flat, patchy areas of light brown pigmentation. These may be found anywhere, but occur most commonly over the buttocks, sacrum, and spine. In unilateral cases, the pigmented areas are often on the same side as the bone lesions.

In females, precocious puberty and endocrine dysfunction are also present, so that it is a common event for these patients to begin to menstruate at the age of two or three years and exhibit fully developed secondary sex characteristics a few years later. Occasionally, precocious bone growth may also be found.

Not all of the component elements of this disease picture are present in all cases. Pigmentation, for example, may be absent. This should not militate against the diagnosis of polyostotic fibrous dysplasia.

LABORATORY FINDINGS

(A) *Blood: 1. Calcium and Phosphorus:* Both the serum calcium and phosphorus are usually within average normal limits in polyostotic fibrous dysplasia. Occasionally, however, when the disease process in the skeletal system is especially

active and diffuse, the serum calcium may be somewhat elevated.

2. Phosphatase: The value for the serum phosphatase may vary considerably. It is usually somewhat elevated and may at times be quite high. Rarely, it may be normal. This can readily be understood, since the level of the serum phosphatase is a reflection of the osteoblastic activity resulting from the stress and strain imposed on the skeletal system by the osseous lesions. The value for the serum phosphatase, then, is roughly proportional to the extent of skeletal involvement. With a diffuse, active process it is fairly high. On the other hand, in the quiescent or healing stage it may be only slightly elevated or even normal.

3. Serum Protein: The total serum protein, as well as the individual fractions of albumin and globulin, is usually normal.

4. Cholesterol: The blood cholesterol is not abnormal in the average case.

(*B*) *Urine: 1. Calcium Excretion:* Usually there is no excessive excretion of calcium in the urine. At times, however, in cases presenting widespread active osseous lesions, hypercalcinuria may be found. Hence, contrary to earlier opinion, the presence or absence of hypercalcinuria is of little value in differentiating between polyostotic fibrous dysplasia and hyperparathyroidism.

2. Estrin Content: The amount of estrogenic substance excreted in the urine is usually within normal limits.

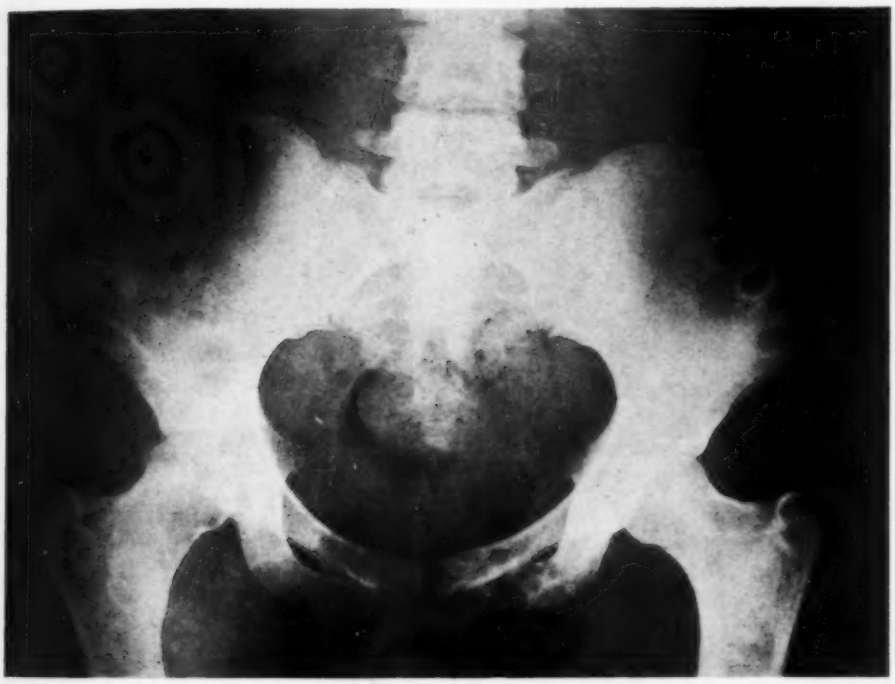


Fig. 2. Case 2: Fibrocystic-like lesions involving the bones of the pelvis.

(*C*) *Basal Metabolic Rate:* The basal metabolic rate is normal unless there is concomitant hyperthyroidism, which occasionally occurs.

(*D*) *Calcium Metabolism:* When patients with polyostotic fibrous dysplasia are placed on a measured low calcium and phosphorus intake, studies usually reveal a positive calcium balance. Obviously, however, in the presence of widespread ac-

tive bone involvement, a negative calcium balance may be found.

ROENTGEN FINDINGS

Although the diagnosis of polyostotic fibrous dysplasia may be suspected clinically, it cannot be established with certainty without a roentgenologic examination. The radiographic appearance of the bone lesions is characteristic. The findings may be summarized as follows:

1. The skeletal involvement has some tendency to be unilateral in distribution, but bilateral lesions are not uncommon.

2. Contrary to the findings in hyperparathyroidism, no generalized decalcification of the bones is present. The lesions are spotty in distribution, consisting of multiple localized areas of diseased bone with normal osseous tissue between.

3. The characteristic lesions are areas of rarefaction resembling bone cysts. These vary considerably in size and shape, and may occur in flat as well as in long bones. The borders of the fibrocystic-like lesions may be sharply defined or gradually fade into the surrounding normal bone tissue. The lesions are not true cysts. The x-ray appearance is due to the replacement of the bone by the fibrous tissue (Figs. 1 and 2).

4. Along with the cyst-like changes, areas of increased density are observed. These vary in extent and may be so pronounced as to result in almost complete obliteration of the medullary canal. Such lesions are particularly prone to occur in the skull, especially at the base, in the region of the floor of the anterior fossa.

5. There is marked thinning of the cortex, along with broadening or expansion of the involved bones. The cortical outline usually remains intact but may occasionally be broken, even in the absence of a pathological fracture (Figs. 3 and 4).

6. Periosteal reaction rarely occurs except at the site of fracture.

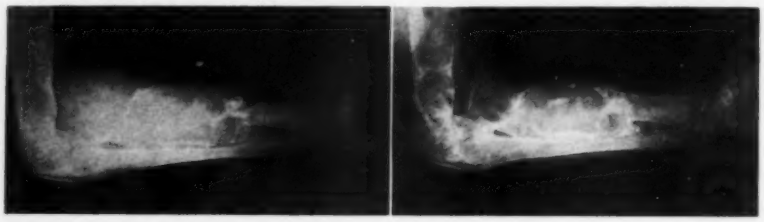
7. Advanced bone age and early epiphyseal union may be present.

8. Frequently, the epiphyses remain intact in the face of diffuse diaphyseal involvement.

9. Various secondary deformities of the involved bones may be present, *e.g.*, coxa vara, bowing of the femur and tibia.

10. Pathological fractures are not uncommon (Fig. 5).

11. The skull is a frequent site of the disease process and may be involved in various ways. (*a*) Irregular dense areas along with the fibrocystic-like involvement may be present, producing a picture not unlike Paget's disease (Fig. 6). (*b*) Extensive sharply demarcated areas of rarefaction may occur, simulating xanthomatosis to some extent. (*c*) The bones of the face and orbit may be involved in a dense, fibrotic process resembling leontiasis ossea (Figs. 7 and 8). (*d*) The mastoid cells and paranasal sinuses may be obliterated by the dense fibrous deposits, and the extension of the disease process into the bones of the face and orbit may lead to facial asymmetry and ocular proptosis.



Figs. 3 and 4. Case 2: The left view shows involvement of the left forearm with dissolution of the cortical continuity of the radius. The right view shows re-establishment of the cortical continuity, increase in calcification, and reduction in swelling of the left forearm following radiation therapy.

PATHOLOGIC ANATOMY

Gross inspection of the involved bones shows them to be expanded and deformed, with pronounced cortical thinning. The medullary canal is replaced by a thick, white, fibrous tissue containing scattered zones of hyaline cartilage.

Microscopic examination reveals the absence of periosteal reaction except in the region of pathologic fractures. The periosteum is represented by a thin fibrous sheet. The normal architectural pattern of both the cortex and medulla has been disrupted as a result of dense fibrous tissue replacement. The latter is composed of fusiform spindle cells with oval, pale-staining nuclei and a vague cytoplasmic outline.

Within the fibrous tissue are irregular small trabeculae of primitive, poorly calcified bone. These trabeculae are often lined by osteoblasts, but there is a noticeable absence of osteoclasts in Howship's lacunae. The trabeculae everywhere appear more or less uniform, being composed of a central structureless matrix enclosing a few cells, surrounded by a peripheral zone of coarsely striped bone. On the surface of some of the trabeculae, thin zones of osteoid tissue may be found. Adjacent to the trabeculae, focal infiltrations of mononuclear cells and lymphocytes may occur.

The fibrous tissue is relatively avascular, with only occasional thin-walled vascular spaces. In some areas, however, there is a larger number of capillaries, especially in the neighborhood of the trabeculae. Granules of hemosiderin may be seen within phagocytes, indicative of previous hemorrhage. In these regions, one may also observe small groups of basophilic, multinucleated giant cells. Most of these are situated within the soft fibrous tissue. A few, however, are located at the periphery of osseous trabeculae, thus suggesting osteoclastic formation. These, in all probability, are not osteoclasts but are due to the coalescence of the cells of the stroma.

Occasional sporadic islets of hyaline cartilage may be found within the fibrous tissue. This cartilage tends to become calcified, especially at its periphery. No lamellated bone is definitely seen, however. At the edge of a lesion, a single trabecula may form the demarcation between normal marrow on one side and dense fibrous tissue on the other. Small cysts may be present, some lined by flattened cells, others without lining.

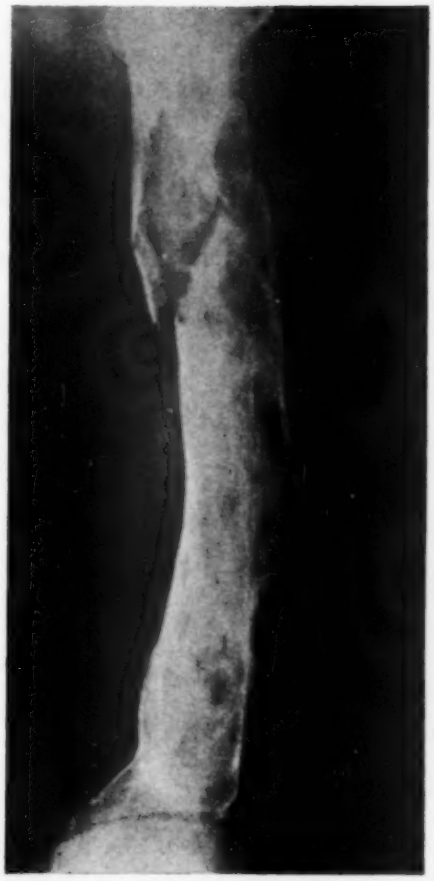


Fig. 5. Case 2: Pathological fracture of the left humerus.

The basic connective tissue varies, being cellular in some regions and resembling mature connective tissue, rich in collagen, in other areas.

DIFFERENTIAL DIAGNOSIS

It is important that polyostotic fibrous dysplasia be differentiated from a number

of conditions which may resemble it to some extent.

Hyperparathyroidism: This disease is the one most readily confused with polyostotic fibrous dysplasia. Careful attention to a few fundamental differences, however, should suffice to make the correct diagnosis. A high serum calcium, a low serum phosphorus, a generalized osteoporosis, and demineralization of the bones are characteristic of hyperparathyroidism. The presence in polyostotic fibrous dysplasia of normal bone between the fibrocystic-like lesions, the tendency toward unilaterality, the areas of pigmentation, and in females the occurrence of precocious puberty and endocrine dysfunction all serve to differentiate this disease from hyperparathyroidism.

Regional Fibrocystic Disease: The exact relationship between polyostotic fibrous dysplasia and regional fibrocystic disease of bone is difficult to determine in the light of our present knowledge. Lichtenstein suggests that localized fibrous lesions of bone may be regarded as a limited form of polyostotic fibrous dysplasia. He also mentions the possibility that there may be multiple skeletal lesions present which are not discovered, since the entire skeletal system is not studied roentgenographically.

Suffice it to say, here, that these two diseases are clinically different. The history, physical findings, and extent of the osseous lesions all serve as differentiating features. Perhaps future investigation will elucidate the true nature of these closely related radiologic patterns.

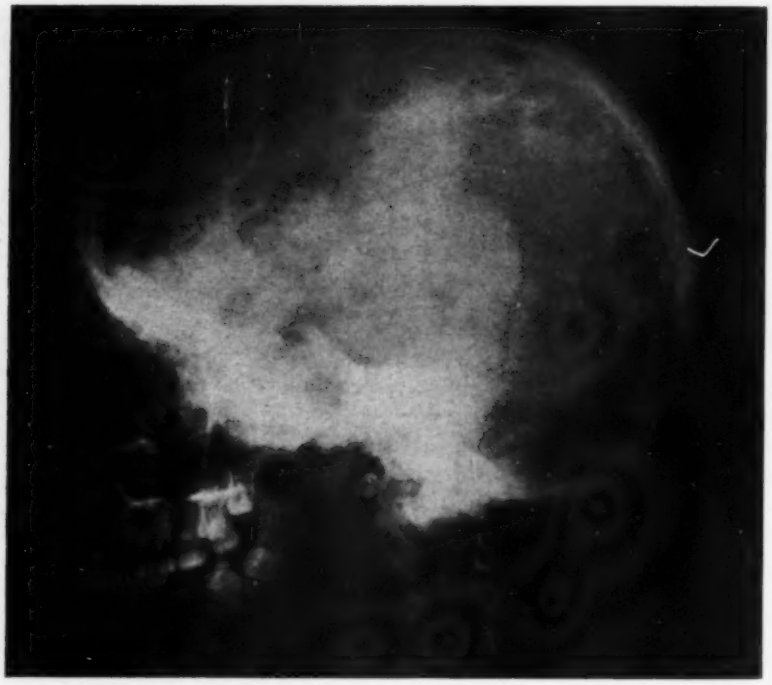


Fig. 6. Case 2: Skull lesions resembling Paget's disease.

Skeletal Enchondromatosis (Ollier's Disease, Dyschondroplasia): In Ollier's disease, there is a tendency for the skeletal lesions to be unilateral, which may cause some superficial resemblance to polyostotic fibrous dysplasia. Otherwise, there should be no difficulty in differentiating

these conditions, since both the clinical course and the x-ray picture are quite different. In polyostotic fibrous dysplasia, there is an absence of macroscopic enchondromata on the metacarpal, metatarsal, and phalangeal joints. Also, in Ollier's disease the symptoms begin in infancy rather than in childhood, as is the case in polyostotic fibrous dysplasia. In addition, the pigmentation, precocious puberty, endocrine dysfunction, and typical fibrocystic bone changes are absent. A biopsy will, of course, readily differentiate these two lesions.

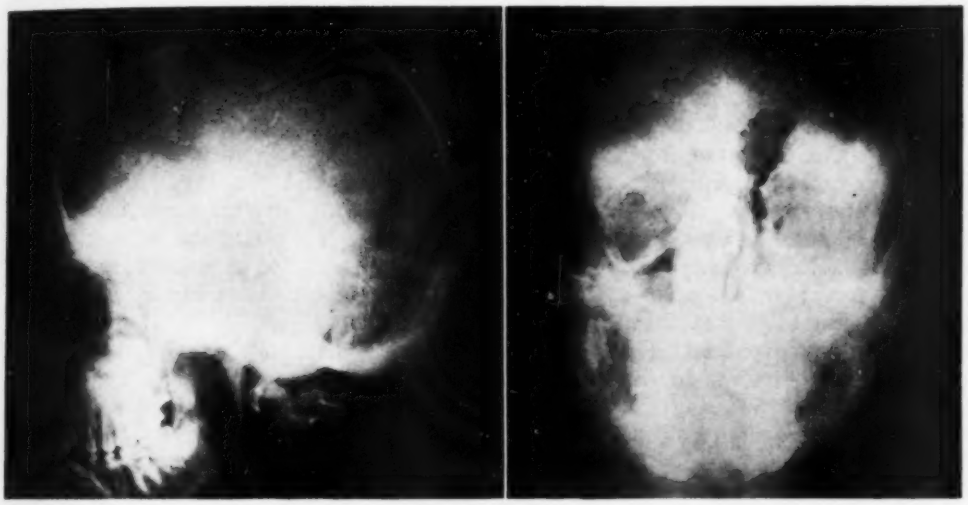
Paget's Disease of Bone: This disease usually occurs in elderly people and bears no clinical resemblance to polyostotic fibrous dysplasia. Roentgenologically, however, the skull in polyostotic fibrous dysplasia may closely resemble that of Paget's disease. In both conditions, there may be dense, fibrous, circumscribed areas, along with regions of rarefaction and a spongy, blotchy appearance, with blurring of the outline of the inner and outer tables.

In the long bones the resemblance is not so marked. Here, thickening of the shaft, increase in size of the bones, cortical involvement, and involvement of the medullary canal are typical of Paget's disease. A biopsy shows no close histologic resemblance between the two conditions.

Leontiasis Ossea: The dense fibrous deposits seen in the skull in some cases of polyostotic fibrous dysplasia constitute the only resemblance to leontiasis ossea. Otherwise, no difficulty is encountered in making the correct diagnosis.

Hand-Schüller-Christian Disease: This disease bears only a superficial similarity to polyostotic fibrous dysplasia, in that there may be large, circumscribed radiolucent areas in the skull in both conditions. The absence of diabetes insipidus and exophthalmos and the presence of the typical clinical and radiographic findings in the long bones, as described above, readily determine the diagnosis of polyostotic fibrous dysplasia.

Bone Cyst: Bone cysts are almost always solitary and have a predilection for the proximal metaphyses of the humerus, femur, and tibia. X-rays show a sharply defined solitary rarefaction with considerable cortical thinning. The solitary lesion, the absence of the typical clinical findings of polyostotic fibrous dysplasia, as well as lack of fibrous lesions and skull involvement, serve to differentiate the benign bone cyst.



Figs. 7 and 8. Case 1: Skull showing dense fibrous overgrowth resembling leontiasis ossea.

Giant-Cell Tumor: This lesion, also, is usually monostotic, having a predilection for the epiphyses of long bones, especially the distal femoral, proximal tibial, proximal humeral, and distal radial epiphyses. The single bone lesion with typical trabeculation, the lack of skull involvement, and the absence of the classical clinical and radiographic picture of polyostotic fibrous dysplasia distinguish the giant-cell tumor.

STATISTICAL SUMMARY AND ANALYSIS[2]

Of a total of 71 cases in the literature in which the sex was specified, 41 (57.3 per cent) occurred in females and 30 (42.7 per cent) in males.

Twenty-nine patients (42 per cent) were between one and ten years of age; 21 (30.4 per cent) were between eleven and twenty; 7 (10.1 per cent) between twenty-one and thirty; 8 (11.6 per cent) between thirty-one and forty; 3 (4.4 per cent) between forty-one and fifty, and 1 (1.5 per cent) over fifty. Five patients (7.0 per cent) gave a history of icterus gravis neonatorum in infancy (81, 8, 53), and 3 (4.2 per cent) had associated hyperthyroidism (81, 5, 53). Interestingly enough parathyroid exploration had been done in 13 (18.3 per cent) because of an erroneous diagnosis of hyperparathyroidism (3, 4, 5, 7, 26, 29, 38, 46, 50, 72, 75).

For 41 of the reported cases no data as to sexual precocity are given. Twenty-two of the females (53 per cent of all the female patients) showed precocious puberty with early onset of the menses. In 5 cases, all in males, there was no evidence of precocious puberty; 1 male (4) had gynecomastia, 1 precocious bone development (4), and 1 hypopituitarism (57).

The percentage of females with associated precocious puberty is, perhaps, not truly representative of the actual incidence, since the association of the bone lesions and endocrine dysfunction was probably not always noted in the earlier reported cases.

Thirty-three patients (46.5 per cent) showed pigmentation; pigmentation was absent in 2 (2.8 per cent), and in the remaining cases no mention of this feature is made.

[2] The figures given here do not include the authors' two cases.

PROGNOSIS AND TREATMENT

Polyostotic fibrous dysplasia is a more or less self-limited disease in the sense that it tends to diminish in activity as the patient grows older. While the affected bones do not return to normal, an equilibrium is reached where the fibrocystic lesions already present tend to become stationary, and no new lesions appear.

The essence of treatment should be conservatism. Curettage and bone grafts are not indicated, since the lesions are so widespread and the same fibrous tissue fills in again. Surgical measures should be limited to the treatment of spontaneous fractures and to osteotomy in selected cases to correct severe bowing of the long bones.

Local radiation therapy has proved of some efficacy and should be employed in the region of progressive bone lesions in an effort to arrest their activity. Preferably, small doses should be employed over a fairly long period of time. It is also possible that irradiation of the pituitary gland may be of some value, in an effort to diminish its activity. This has not been employed, to the knowledge of the authors. It is now undergoing a trial.

The patient should, of course, be warned against undue trauma and severe exercise because of the tendency to spontaneous fracture.

TERMINOLOGY

Polyostotic fibrous dysplasia has been described in the literature under a multiplicity of terms—regional fibrocystic disease, focal osteitis fibrosa, osteitis fibrosa in multiple foci, osteitis fibrosa with formation of hyaline cartilage, osteitis fibrosa disseminata, unilateral von Recklinghausen's disease, unilateral osteitis fibrosa cystica generalisata, unilateral polyostotic osteitis fibrosa, osteodystrophia fibrosa unilateralis, osteodystrophia fibrosa cystica

generalisata limited to one side of the body, osteodystrophia fibrosa, generalized osteitis fibrosa cystica not due to hyperparathyroidism, juvenile Paget's disease, Albright's disease. The continued employment of so many different terms must inevitably produce further chaos.

Some of the confusion may be attributed to the indiscriminate use in the German literature of the terms osteitis fibrosa and fibrous osteodystrophy to describe the osseous lesions of Paget's disease, bone cyst, giant-cell tumors, hyperparathyroidism, and localized osteitis fibrosa. Such a practice is greatly to be deplored, and can only lead to confusion.

The term polyostotic fibrous dysplasia was originally introduced by Lichtenstein in 1938. It is not a particularly good descriptive term, since in its literal sense it includes any fibrous dysplasia involving multiple bones, *e.g.*, Paget's disease, hyperparathyroidism, etc. It has, however, gained such wide acceptance and usage that it would probably be wise to keep it, to avoid the further confusion which would inevitably result from the introduction of still another name.

CASE REPORTS

CASE 1: L. G., a 15-year-old white male, was a full term normal infant, spontaneously delivered. No icterus neonatorum was present. The family history is significant only in so far as the elder of the patient's two sisters had "sleeping sickness" as a child.

Early in childhood, the patient suffered a head injury as a result of a fall. At the age of five, his mother first noticed that the right side of his face was more prominent than the left. Except for frequent colds and sore throats, however, he remained essentially well until September 1937, when, at the age of 10, he fell and fractured his right elbow. He was seen in the out-patient department of the Newark Beth Israel Hospital on Nov. 11, 1937. At that time, physical examination revealed a facial asymmetry (right side more prominent than the left), some limitation of motion of the right elbow, along with evidence of radial nerve and partial median nerve involvement on the affected side. No pigmentation or endocrine disturbances were present. The remainder of the physical examination was essentially negative.

X-ray examination disclosed an old, well united supracondylar fracture of the right humerus, with some internal angulation at the fracture site. The roentgenologist suggested that the fracture was probably pathological, because of a multiloculated, cystic appearance of the lower end of the shaft of the right humerus. There was also an alteration in structure of the radius and ulna on this side. Similar changes were noted in the left humerus, radius, and ulna. At this time, a tentative diagnosis of osteitis fibrosa cystica (von Recklinghausen) was made.

Further x-ray studies showed bone lesions involving the skull, ribs, both humeri, radii, ulnae and hands, both femora, right tibia and fibula, both feet, and the lumbar spine. In 1938, the diagnosis of polyostotic fibrous dysplasia was made, and was later confirmed by Dr. Henry Jaffe. In 1941, it was noted that the patient had between three and four diopters of choking of the right disc, due to pressure on the optic nerve from the fibrous involvement of the skull. At this time, his vision was O.D.—15/20; O.S.—15/15. Examination of the visual fields revealed no abnormality. Because it was felt that the disease is more or less self-limited and tends to regress at puberty, it was decided to watch the patient closely rather than attempt immediate surgical intervention to relieve the pressure on the optic nerve. Repeated examinations to date have shown no progression of the ocular findings.

At the present time, the patient is quite well, attends school, and has had a normal growth and development. His bone lesions show no evidence of progression and appear to be stable.

Successive serum calcium and phosphorus studies in this case gave the following figures:

	4/15/38	7/15/39	2/15/41	9/20/41	2/16/42	4/23/42
Calcium (mg. per 100 c.c.)	11.4	11.0	10.5	10.1	10.9	9.6
Phosphorus (mg. per 100 c.c.)	4.4	3.9	4.2	4.8	4.7	2.5
Phosphatase (Bodansky units)	19.1	..	8.3	2.6	15.7	22.1

Ionizable fraction of serum calcium (calculated from total serum calcium and serum proteins according to the nomogram of McLean and Hastings): 4.5 (within normal limits).

Serum proteins were 6.3 gm. per 100 c.c.; cholesterol, 272 mg. per 100 c.c. The glucose tolerance test was normal and the Wassermann and Kline tests were negative. Hemoglobin was 13.9 gm.; red cell count 4,650,000; white cell count 9,500, with 46 per cent polymorphonuclears, 45 per cent lymphocytes, 5 per cent mononuclears, 1 per cent eosinophils, and 3 per cent stab forms.

Sternal marrow puncture showed 112,200 nucleated cells per cubic millimeter; segmented neutrophils, 21; non-segmented neutrophils, 19; lymphocytes, 19; eosinophils, 1; eosinophilic myelocytes, 1; myelocytes, 21; blasts, 4; plasma cells, 1; gones, 11; normoblasts, 58 per 100 white blood cells; erythroblasts, 7 per 100 white cells. The findings were interpreted as evidence of myelophthisis due to encroachment on the marrow space.

The urine was essentially negative, with no hypercalcinuria.

CASE 2: E. M., a 17-year-old white female, was first seen at the Newark Beth Israel Hospital on April 14, 1941, having been hospitalized on five previous occasions at two other hospitals. She had been a full-term, spontaneously delivered, normal infant, and gave an essentially negative family history. Five siblings were all alive and well. During early childhood, the patient had measles, whooping cough, mumps, chickenpox, and frequent sore throats (all uncomplicated).

At the age of three, she suffered a head injury as the result of a fall. Shortly thereafter she began to menstruate, vaginal bleeding occurring two or three times a year and lasting two to three days. At five years of age, there was a cessation of the menses until the age of nine, when they returned, along with full maturation of the secondary sex characteristics. At this time, she bumped her left elbow against a door. A month later her father noticed a swelling of her left lower arm and upper forearm, associated with stiffness and pain in the elbow joint. Roentgen and biopsy studies of the left humerus led to a diagnosis of osteitis fibrosa cystica.

In 1935 (when the patient was ten), a parathyroid exploration was done and one parathyroid gland was removed. Microscopic examination of the latter showed normal parathyroid tissue. In 1938 the lower third of the left humerus was fractured as a result of a fall.

During the latter part of 1940, pain, swelling, and tenderness of the left forearm developed, persisting until the patient's admission to the Newark Beth Israel Hospital, April 14, 1941. Physical examination at that time showed a well nourished, well developed, intelligent girl with slight ptosis of the left upper eyelid and a bony prominence above the upper outer margin of the left orbit. There was an area of brown pigmentation in the skin of the back, overlying the region of the twelfth dorsal vertebra (2 1/2 inches long by 1/2 inch wide). A similar area was present in the gluteal region, between the folds of the buttocks. The left lower arm and proximal forearm were the site of considerable swelling, which was painless and brawny. In addition, there was partial limitation of motion of the left elbow joint. The remainder of the physical examination was essentially negative.

Roentgenograms showed extensive disease of the entire skeleton. The patient received a fairly large dose of x-ray therapy directed to the region of the left forearm and upper arm. The radiation therapy was given over a prolonged period, with several rest intervals. The total dosage was 5,200 r over a period of one year. Following radiation therapy, the swelling and induration of the left upper extremity diminished considerably.

On March 14, 1942, the patient was readmitted to the hospital because of a fracture of the left upper humerus as the result of a fall. At this time, further x-ray therapy was given to the left humerus (1,200 r in divided doses). The fracture healed fairly rapidly and on April 23, 1942, there was good firm union at the fracture site.

At present, the patient is being observed in the out-patient department. She leads a fairly normal life except for abstinence from severe exercise.

Serum calcium and phosphorus determinations were as follows:

	11/11/34	10/35	11/40	4/15/41	7/8/41	9/10/41	3/16/42	3/23/42
Calcium (mg. per 100 c.c.)	8.5	11.3	10	9.8	10.9	10.0	10.5	9.6
Phosphorus (mg. per 100 c.c.)	3.1	3.0	3.4	3.3	3.2	2.6	2.6	3.9
Phosphatase (Bodansky units)	...	..	..	14.3	17.2	16.8	17.6	11 9

Ionizable fraction of serum calcium: 5.0 (within normal limits).

The results of other laboratory studies were as follows: serum proteins, 6.4 gm. per 100 c.c.; cholesterol, 200 mg. per 100 c.c.; blood sugar 88 mg. per 100 c.c.; blood urea nitrogen, 10 mg. per 100 c.c.; Wassermann and Kline tests, negative; hemoglobin, 90 per cent; red blood cells 4,800,000; white cells, 7,900 with 62 per cent polymorphonuclears 28 per cent lymphocytes, 3 per cent monocytes, and 7 per cent stab forms.

The urine was essentially negative, with no hypercalcinuria.

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201 Lyons Ave.
Newark, N. J.

BIBLIOGRAPHY

1. ABELOFF, A. J., SOBEL, S. P., AND BERNHARD, A.: Extensive Decalcification of Bones in an Eight Year Old Boy. Am. J. Dis. Child. **45:** 105-113, January 1933.

2. ADAMS, C. O., COMPERE, E. L., AND JEROME, J.: Regional Fibrocystic Disease. Surg., Gynec. & Obst. **71:** 22-32, July 1940.

3. ALBRIGHT, F., BUTLER, A. M., HAMPTON, A. O., AND SMITH, P.: Syndrome Characterized by Osteitis Fibrosa Disseminata, Areas of Pigmentation and Endocrine Dysfunction, with Precocious Puberty in Females: Report of Five Cases. New England J. Med. **216:** 727–746, April 29, 1937.

4. ALBRIGHT, F., SCOVILLE, W. B., AND SULKOWITCH, H. W.: Syndrome Characterized by Osteitis Fibrosa Disseminata, Areas of Pigmentation, and Gonadal Dysfunction: Further Observations Including Report of Two More Cases. Endocrinology **22:** 411–421, April 1938.

5. BARNWELL, R.: Cited by Albright, Scoville, and Sulkowitch (4).

6. BENTZON, P. G. K.: Roentgenologic and Experimental Studies on the Pathogenesis of Dyschondroplasia. Acta radiol. **3:** 89, 1924.

7. BORAK, J., AND DOLL, B.: Unilateral von Recklinghausen's Disease of Bone with Precocious Puberty. Wien. klin. Wchnschr. **47:** 540, 1934.

8. BRAID, F.: Osseous Dystrophy Following Icterus Gravis Neonatorum; Generalized Osteitis Fibrosa with Areas of Pigmentation of Skin and Precocious Puberty in Female. Arch. Dis. Childhood **14:** 181–202, September 1939.

9. BRAID, F.: Osseous Dystrophy Following Icterus Gravis Neonatorum. Arch. Dis. Childhood **7:** 313–320, December 1932.

10. BROOKS, C. M.: Studies on the Neural Bases of Ovulation in the Rabbit. Am. J. Physiol. **113:** 18, 1935.

11. BROOKS, B., AND LEHMAN, E. P.: Bone Changes in Recklinghausen's Neurofibromatosis. Surg., Gynec. & Obst. **38:** 587–595, May 1924.

12. BUCHBINDER, W. C., AND KERN, R.: Blood Calcium Deficiency in Experimental Obstructive Jaundice. Am. J. Physiol. **80:** 273–277, April 1927.

13. BUCHBINDER, W. C., AND KERN, R.: Experimental Obstructive Jaundice: Growth Factor in Defective Calcification. Arch. Int. Med. **40:** 900–910, December 1927.

14. BUCHBINDER, W. C., AND KERN, R.: Experimental Obstructive Jaundice: Modification of Parathyroid Tetany Mechanism in Jaundice. Arch. Int. Med. **41:** 754–763, 1928.

15. COLEMAN, M.: Osteitis Fibrosa Disseminata: Case. Brit. J. Surg. **26:** 705–713, April 1939.

16. COSACESCO, A.: Fibrocystic Osteitis Localized on One Side. Rev. de chir., Bucuresti **43:** 313–316, May-June 1940.

17. CROUZON, O., BRAUN, S., AND DELAFONTAINE, P.: Osteitis Deformans in Mother; Undetermined Osseous Dystrophy in Daughter. Bull. et mém. Soc. méd. d. hôp. de Paris **50:** 1754–1759, Dec. 30, 1926.

18. DENSTAD, T.: Polyostotic Fibrous Dysplasia. Acta radiol. **21:** 143–150, 1940.

19. DIEZ, J.: Albright's Syndrome (Disseminated Osteitis Fibrosa with Precocious Puberty and Cutaneous Pigmentation). Bol. y trab. Soc. de cir. de Buenos Aires **23:** 462–481, July 19, 1939.

20. Editorial: Polyostotic Fibrous Dysplasia. Am. J. Roentgenol. **47:** 161–162, January 1942.

21. ELMSLIE, R. C.: Fibrosis of Bone: Generalized Osteitis Fibrosa Cystica Not Due to Hyperparathyroidism. St. Bartholomew's Hosp. Rep. **68:** 147–158, 1935.

22. FAIRBANK, H. A. T.: Discussion on Fibrocystic Disease of Bone. Proc. Roy. Soc. Med. **27:** 977–978, 1934.

23. FORD, F. R., AND GUILD, H.: Precocious Puberty Following Measles Encephalomyelitis and Epidemic Encephalitis, with Discussion of Relation of Intracranial Tumors and Inflammatory Processes to Syndrome of Macrogenitosomia praecox. Bull. Johns Hopkins. Hosp. **60:** 192–203, March 1937.

24. FRANGENHEIM, P.: Osteitis Fibrosa in Childhood. Beitr. z. klin. chir. **76:** 227, 1911.

25. FREEDMAN, H. J.: Disturbance of Function of the Suprarenal Glands in Children. Am. J. Dis. Child. **44:** 1285–1292, December 1932.

26. FREUND, E.: Osteodystrophia Fibrosa Unilateralis: Case. Arch. Surg. **28:** 849–866, May 1934.

27. FREUND, E., AND MEFFERT, C. B.: On the Different Forms of Non-Generalized Fibrous Osteodystrophy: Localized, Diffuse Monostotic, Unilateral and Monomelic Form. Surg., Gynec. & Obst. **62:** 541–561, March 1936.

28. FRIEDGOOD, H. B., AND PINCUS, G.: Studies on Conditions of Activity in Endocrine Organs: Nervous Control of the Anterior Hypophysis as Indicated by Maturation of Ova and Ovulation after Stimulation of the Cervical Sympathetics. Endocrinology **19:** 710–718, November-December 1935.

29. GARLOCK, J. H.: Differential Diagnosis of Hyperparathyroidism, with Special Reference to Polyostotic Fibrous Dysplasia. Ann. Surg. **108:** 347–361, September 1938.

30. GAUPP. V.: Precocious Puberty in Osteodystrophia Fibrosa. Monatschr. f. Kindh. **53:** 312–322, 1932.

31. GOLDHAMER, K.: Osteodystrophia Fibrosa Unilateralis (Associated with Pubertas praecox and Osteosclerotic Changes in the Skull). Fortschr. a. d. Geb. d. Röntgenstrahlen **49:** 456–481, May 1934.

32. GREEP, R. O.: Functional Pituitary Grafts in Rats. Proc. Soc. Exper. Biol. & Med. **34:** 754–755, June 1936.

33. GREEP, R. O., FEVOLD, H. L., AND HISAW, F. L.: Effects of Two Hypophyseal Gonadotropic Hormones on the Reproductive System of the Male Rat. Anat. Rec. **65:** 261–271, June 25, 1936.

34. HEARD, J. D., SCHUMACHER, F. L., AND GORDON, W. B.: Association of Diabetes Insipidus with Osteitis Fibrosa Polycystica. Am. J. M. Sc. **171:** 38–48, January 1926.

35. HIMMELMAN, W.: Hypogenitalism and Hyperparathyroidism and Disturbances of Calcium Metabolism in Localized Osteodystrophia Fibrosa. Klin. Wchnschr. **9:** 2443, Dec. 27, 1930.

36. HIRSCH, I. S.: Is Generalized Osteitis Fibrosa (Paget and von Recklinghausen) Congenital? Am. J. Surg. **3:** 167–175, August 1927.

37. HIRSCH, I. S.: Generalized Osteitis Fibrosa. Radiology **13:** 44–84, July 1929.

38. HORWITZ, T., AND CANTAROW, A.: Polyostotic Fibrous Dysplasia: Case. Arch. Int. Med. **64:** 280–285, August 1939.

39. HUMMEL, R.: Two Cases of Juvenile Osteitis Deformans (Paget's). Röntgenpraxis **6:** 513–519, August 1934.

40. HUNTER, D., AND TURNBULL, H. M.: Hyperparathyroidism: Generalized Osteitis Fibrosa, with Observations upon Bones, Parathyroid Tumours, and Normal Parathyroid Glands. Brit. J. Surg. **19:** 203–284, October 1931.

41. HUNTER, D., AND WILES, P.: Dyschondroplasia (Ollier's Disease). Brit. J. Surg. **22:** 507–519, January 1935.

42. IVIMEY, M.: Bone Dystrophy with Characteristics of Leontiasis Ossea, Osteitis Deformans, and Osteitis Fibrosa Cystica in Child; Suggestion as to Influence of Central Nervous System. Am. J. Dis. Child. **38:** 348–360, August 1929.

43. JAFFE, H. L.: Atypical Form of Paget's Disease Appearing as Generalized Osteosclerosis. Arch. Path. **16:** 769–794, December 1933.

44. JAFFE, H. L., BODANSKY, A., AND CHANDLER, J. P.: Ammonium Chloride Decalcification as Modified by Calcium Intake: Relation between Generalized Osteoporosis and Ostitis Fibrosa. J. Exper. Med. **56:** 823–834, December 1932.

45. JANSEN, M.: Dissociation of the Growth Process in Bones. Verhandl. Deutsch. orthop. Gesellsch. **49:** 274, 1927.

46. JOHNSON, G. M.: Hyperparathyroidism with von Recklinghausen's Osteitis Fibrosa Cystica Generalisata and Hypopituitarism. Am. J. Surg. **32:** 113–115, April 1936.

47. KALLIUS, H. U.: Etiology of Generalized Osteodystrophia Fibrosa: Experimental and Theoretic Studies. Arch. f. klin. Chir. **169:** 466–476, 1932.

48. KORNBLUM, K.: Polyostotic Fibrous Dysplasia. Am. J. Roentgenol. **46:** 145–159, August 1941.

49. LEADER, S. D., AND GRAND, M. J. H.: Von Recklinghausen's Disease in Children: Report of a Case Presenting Cutaneous Pigmentation and Bone Changes. J. Pediat. **1:** 754–763, December 1932.

50. LICHTENSTEIN, L.: Polyostotic Fibrous Dysplasia. Arch. Surg. **36:** 874–898, May 1938.

51. MANDL, F.: Clinical and Experimental Studies of the Problem of Localized and Generalized Osteitis Fibrosa. Arch. f. klin. Chir. **143:** 1–46, 1926.

52. MARX, J.: Effect of Hormones of Thymus and Spleen on Osteodystrophy. Zentralbl. f. Chir. **63:** 208–212, Jan. 25, 1936.

53. MCCUNE, D. J.: Osteitis Fibrosa Cystica. Am. J. Dis. Child. **52:** 745, 1936.

54. MCCUNE, D. J., AND BRUCH, H.: Osteodystrophia Fibrosa: Report of a Case in Which the Condition Was Combined with Precocious Puberty, Pathologic Pigmentation of Skin, and Hyperthyroidism, with a Review of the Literature. Am. J. Dis. Child. **54:** 806–848, October 1937.

55. MCLEAN, F. C., AND HASTINGS, A. B.: Clinical Estimation and Significance of Calcium-Ion Concentrations in the Blood. Am. J. M. Sc. **189:** 601–613, May 1935.

56. MEYER-BORSTEL, H.: Osteitis (Osteodystrophia) Fibrosa: Cases. Beitr. z. klin. Chir. **148:** 436, 510, 1930.

57. MOEHLIG, R. C., AND SCHREIBER, F.: Polyostotic Fibrous Dysplasia: Report of Case with Unilateral Involvement. Am. J. Roentgenol. **44:** 17–23, July 1940.

58. MONDOR, H., DUCROQUET, R., LÉGER, L., AND LAURENCE, G.: Unilateral Fibrocystic Osteitis with Pigmentation and Precocious Puberty. Rev. gén. de clin. et de thérap. **52:** 823–824, Dec. 10, 1938.

59. MONDOR, H., DUCROQUET, R., LÉGER, L., AND LAURENCE, G.: Disseminated Fibrogeodic Osteitis with Cutaneous Pigmentation and Precocious Puberty: Relation between Recklinghausen's Osteitis and Recklinghausen's Neurofibromatosis. J. de chir. **53:** 593–624, May 1939.

60. MOORE, B. H.: Some Orthopaedic Relationships of Neurofibromatosis. J. Bone & Joint Surg. **23:** 109–140, January 1941.

61. MORTIMER, H.: Influence of the Anterior Pituitary on Cranial Form and Structure and the Significance of Cranial Dysplasia in Clinical Diagnosis. Chapter VIII in The Pituitary Gland, Baltimore, Williams & Wilkins Co., 1938.

62. NÄGELSBACH, E.: Fatal Case of Generalized Osteitis Fibrosa with Disturbances of the Internal Secretions. Fortschr. a. d. Geb. d. Roentgenstrahlen **31:** 82–86, 1923.

63. NELLER, J. L.: Osteitis Fibrosa Cystica (Albright). Am. J. Dis. Child. **61:** 590–605, March 1941.

64. NORDRUM, F.: Generalized Fibroid Osteitis in a Woman. Norsk. Mag. f. Laegevidensk. **87:** 615–622, July 1926.

65. PARHON, C. I., AND KREINDLER, A.: Osteodystrophic Phenomena Associated with Sexual Disturbances: Diminution of Muscular Chronaxia. Bull. et mém. sect. d. endocrinol. **1:** 202–205, November 1935.

66. PHEMISTER, D. B., AND GRIMSON, K. S.: Fibrous Osteoma of the Jaws. Ann. Surg. **105:** 564–583, April 1937.

67. PHILIPS, H. B.: Paget's Disease. J. Bone & Joint Surg. **8:** 643–650, July 1926.

68. PRIESEL, R., AND WAGNER, R.: Osteitis Fibrosa Cystica Generalisata. Ztschr. f. Kinderh. **53:** 146–161, 1932.

69. REUBEN, M. S., AND MANNING, G. R.: Precocious Puberty. Arch. Pediat. **39:** 769–785, Dec. 22, 1922.

70. REUBEN, M. S., AND MANNING, G. R.: Precocious Puberty. Arch. Pediat. **40:** 27–44, 1923.

71. ROBBINS, C. L.: Osteitis Fibrosa Cystica and Renal Calculi without Hypercalcemia. J. A. M. A. **104:** 117–118, Jan. 12, 1935.

72. ROBSON, K., AND TODD, J. W.: Fibrocystic Disease of Bone with Skin Pigmentation and Endocrine Dysfunction. Lancet **1:** 377–380, Feb. 18, 1939.

73. RYPINS, E. L.: Osteitis Fibrosa Cystica at Unusual Age. J. Bone & Joint Surg. **15:** 509–512, April 1933.

74. SALZER, H.: Case of Unilateral Osteitis Fibrosa Cystica Generalisata. Wien. klin. Wchnschr. **27:** 862, 1933.

75. SHELLARD, B. T.: Osteitis Fibrosa Disseminata. M. J. Australia **1:** 558–560, 1940.

76. SMITH, P. E., AND DORTZBACH, C.: First Appearance in Anterior Pituitary of Developing Pig Foetus of Detectable Amounts of Hormones Stimulating Ovarian Maturity and General Body Growth. Anat. Rec. **43:** 277–294, Aug. 29, 1929.

77. SCHAPPER, I., AND PARISEL, C.: Xanthomatosis Generalisata Ossium. Quart. J. Med. **2:** 407–417, July 1933.

78. SOPHIAN, A.: Diabetes Insipidus and Osteitis Fibrosa Polycystica. J. A. M. A. **95:** 483–484, Aug. 16, 1930.

79. STALMANN, A.: Nerve, Skin, and Bone Changes in v. Recklinghausen's Neurofibromatosis and Their Developmental Relationship. Virchows Arch. f. path. Anat. **289:** 96–126, 1933.

80. STAUFFER, H. M., ARBUCKLE, R. K., AND AEGERTER, E. E.: Polyostotic Fibrous Dysplasia with Cutaneous Pigmentation and Congenital Arteriovenous Aneurysms: Case. J. Bone & Joint Surg. **23:** 323–334, April 1941.

81. SUMMERFELDT, P., AND BROWN, A.: Osteodystrophia Fibrosa. Am. J. Dis. Child. **57:** 90–101, January 1939.

82. SVÅB, V.: Osteodystrophia Fibrosa Cystica Generalisata: Roentgenologic Study of Two Cases. Fortschr. a. d. Geb. d. Röntgenstrahlen **55:** 450–457, May 1937.

83. TELFORD, E. D.: Case of Osteitis Fibrosa with Formation of Hyaline Cartilage. Brit. J. Surg. **18:** 409–414, January 1931.

84. THOMAS, H. W., MEREDITH, T. N., AND WUNDERLY, H. L.: Osteodystrophia Disseminata: Case. J. Pediat. **18:** 638–642, May 1941.

85. TOBLER, W.: Generalized Cystic Fibrous Osteitis in Children. Ztschr. f. Kinderh. **41:** 334–335, 1926.

86. VON BEUST, A. T.: Osteitis Fibrosa and Bone Cysts in Congenital Fracture of Lower Leg. Deutsche Ztschr. f. Chir. **152:** 60–89, 1920.

87. VAN BOGAERT, L.: Hereditary and Familial Form of Paget's Osteitis Deformans with Chorioretinitis Pigmentosa. Ztschr. f. d. ges. Neurol. u. Psychiat. **147:** 327–345, 1933.

88. VICKERS, W., AND TIDSWELL, F.: Tumor of the Hypothalamus. M. J. Australia **2:** 116–117, July 23, 1932.

89. VON HABERER, H.: Problem of Bone Cysts and Osteitis Fibrosa. Arch. f. chir. **82:** 873, 1907.

90. VON RECKLINGHAUSEN, F. D.: Tumor-form-

ing Osteitis Fibrosa, Festschrift, R. Virchow, Berlin, 1891, p. 81.

91. VON RECKLINGHAUSEN, F. D.: Multiple Fibromas of the Skin and Their Relationship to Multiple Neuromas. Berlin, Hirschwald, 1882.

92. WEBER, F. P.: Note on Syndromes Sometimes Associated with Retinitis Pigmentosa and Pigmentary Incomplete Forms of Recklinghausen's Disease. M. Press **119:** 416–419, 1925.

93. WEBER, F. P., AND PERDRAU, J. R.: Periosteal Neurofibromatosis. Quart. J. Med. **23:** 151–166, 1930.

94. WEIL: Precocious Puberty and Bone Brittleness. Klin. Wchnschr. **1:** 2114, 1922.

95. WEISS, K.: Unilateral Variety of Multiple Chondromata. Fortschr. a. d. Geb. d. Roentgenstrahlen **31:** 615, 1923–24.

96. WEISSENBACH, R. J., AND LIÈVRE, J. A.: Osteitis Fibrosa without Parathyroid Adenoma. Presse méd. **47:** 260–262, Feb. 18, 1939.

97. WERNER, A. A.: Endocrinology: Clinical Application and Treatment. Philadelphia, Lea & Febiger, 1937.

98. WIELAND, E.: Osteitis Fibrosa Cystica Congenita. Arch. f. Kinderheilkunde **71:** 241–263, August 1922.

99. WINTER, H.: Generalized Osteitis Fibrosa without Tumor of Parathyroids: Case. Zentralbl. f. Chir. **56:** 2647–2649, Oct. 19, 1929.

100. WOLF, WILLIAM: Endocrinology in Modern Practice. Philadelphia, W. B. Saunders Co., 1936.

EDITORIAL

Howard P. Doub, M.D., Editor

John D. Camp, M.D., Associate Editor

Treatment of Carcinoma of the Cervix Uteri

If a generalization is warranted regarding the treatment of any malignant neoplasm, it is that carcinoma of the cervix should always be treated by irradiation. This is the teaching in all the reputable medical journals and medical schools, and the judgment of those physicians who have most to do with the care of this disease. This does not mean that the occasional case cannot be adequately cared for by proper surgery, but far too often the patient's chance of recovery has been lost because of ill-advised and inadequate surgical procedure. Many women with carcinoma of the cervix are still operated on by the general surgeon with notoriously poor results, and the too prevalent practice of amputating the cervix for carcinoma cannot be too strongly condemned.

Since the foregoing is true, it means that the competent radiologist or the gynecologist trained in irradiation therapy should treat all proved cases of cervical carcinoma. These physicians, of course, must have had training and experience and must be conversant with the physical factors that affect depth dose and be able to estimate with a reasonable degree of accuracy the amount of radiation delivered to the tumor. Not only should this be true for external irradiation, but also for transvaginal roentgen therapy and the intravaginal and intrauterine application of radium. It should be understood by all who treat these lesions that figures will not arrest malignant disease—that only delivered dosage is effective. Therefore, the designation of roentgen dosage as a summation of the air doses to the several ports and that of radium as milligram hours does not give an adequate concept of the treatment given. More and more of us are now realizing that it is necessary to figure tumor dose delivered through external ports. So far, however, there is no general appreciation of the fact that the same physical factors apply to radium and that milligrams times hours is not in itself a true indication of the radium dosage.

Since for the present we must assume that effect on the tumor is dependent primarily on delivered radiation, it behooves us to use every means at our disposal to increase this amount within the limits of tolerance of normal tissue. More and more must we realize that adequate irradiation for carcinoma of the cervix is a major procedure and that to increase the percentage of five-year survivals we must increase the complications resulting from the treatment. This may be in the form of skin, bowel and bladder reactions, or even the rare irradiation fractures of the femoral neck. The possibility of the development of these complications should not deter us from giving maximum doses. This attitude has enabled some radiologists to increase the five-year survivals 100 per cent in the past ten years. With heavy irradiation one can now expect up to 40 per cent five-year survivals, when all groups are taken together.

That some radiologists and gynecologists are taking the problem seriously can be seen by the papers presented as a symposium in this issue of RADIOLOGY. It has been a far cry from the first attempts to influence carcinoma of the cervix by

means of external irradiation with low voltage and light filtration to present-day therapy using 200 kv., heavy filtration, and multiple ports. Significant work is also being done with roentgen rays generated at higher voltage, although most of us for economic reasons will have to be content with lower voltages. Only recently, however, have we begun to use the maximum dosage possible with 200 kv. The advent of shock-proof apparatus has also made possible satisfactory application of roentgen rays direct to the primary lesion, with excellent results.

Although all of us hope that education of the laity and the profession regarding the treatment of cancer will result in our seeing neoplasms of the cervix in an earlier stage of development, our therapeutic problem remains the same. If we fail to do our utmost, we are culpable.

H. DABNEY KERR
University Hospital
Iowa City, Iowa

ANNUAL MEETING RADIOLOGICAL SOCIETY OF NORTH AMERICA

Attention is again called to the 1943 Meeting of the Radiological Society of North America, which according to present plans will be held at the Drake Hotel, in Chicago, Nov. 29–Dec. 3, 1943.

New problems created by war and the additional responsibilities placed upon the radiologist make it more important than ever that he avail himself of every opportunity to profit by the experiences of others and share with them his own observations, whether in military or civilian practice. It is hoped that the 1943 meeting may equal that of 1942 in attendance and enthusiasm.

NO RATIONING OF X-RAY FILMS

The following *Bulletin* of the American College of Radiology, dated April 15, is of such immediate interest to all radiologists that it is reprinted here.

"There will be no rationing of x-ray films. Private radiologists will enjoy the same rights as hospitals and clinics in obtaining films; no preferential treatment will be given to hospitals. There is an abundance of materials required in the manufacture of roentgen film. Productive facilities are taxed to the utmost. Although reduced supplies will be available, there is no expectation of an acute shortage.

"These are the facts obtained by the A.C.R. in the investigation of a threatened shortage of roentgen films which developed last month. Members from many sections of the country reported difficulty in obtaining films. Rumors spread that private physicians would be denied films and that the reduced supply which would be available would be allocated to hospitals.

"It is true that a temporary shortage developed. Three factors were responsible: (1) The Army and Navy placed orders for huge supplies. (2) No one foresaw the tremendous demand of industry for films required in industrial roentgenography (many Army-Navy contracts specified, for instance, that each casting of a particular part be examined roentgenographically). (3) Hospitals took advantage of a preferred rating which enabled them to purchase a three months' supply of films in advance of other orders without priority.

"On March 19, the WPB issued Controlled Materials Plan Regulation 5A. Under this order hospitals were given a priority of AA-1 for the purchase of maintenance, repair, and operating supplies. A subsequent interpretation by the WPB placed x-ray films under the order. Originally intended to protect hospitals against breakdowns and exhaustion of supplies necessary for maintenance, the order gave them the privilege of obtaining, in any three-month period, 30 per cent of the total number of films used in 1942. Orders placed under the top priority rating they possessed had to be filled before all others. This, together with the other two factors mentioned above, made it difficult for private physicians in many localities to obtain all the films they wanted or needed.

"Immediately the situation became clear, the College communicated with WPB officials with the request that prompt action be taken. A meeting was held in Washington on April 9. Next day the College was assured by telegram from the WPB that the supply of films was sufficient to meet demands and that they would not be rationed. Moreover, we are advised from other sources that films will be excluded from CMPR 5A, and that private radiologists will enjoy the same privileges as hospitals in obtaining films."

INTER-AMERICAN RADIOLOGICAL CONVENTION

The following letter has recently been received by the Secretary of the Radiological Society of North America:

My Distinguished Colleague:

As President of the Radiological Society in Argentina, I have the pleasure of informing you that this Society is organizing, on its own initiative, the First Inter-American Radiological Convention, to be held in Buenos Aires in October of 1943.

I am confident that this initiative, which I am sure will be the beginning of a friendship marked by closer union of the radiologists of all the Americas, will meet with your enthusiastic approval. I would very much appreciate your making it known to all the members of your Society, whom we have the pleasure of inviting to attend and participate as official narrators.

The elected subjects are the following:

"Roentgen Diagnosis of Spinal Diseases"
"Breast Cancer: Its Treatment and Results"
"X-ray Diagnosis of the Intestinal Diseases" (including inflammation of the jejunum and ileum and inflammation of the colon).

For each subject there will be two or more official narrators. For the first one, Dr. Di Rienzo (of Córdoba, Argentina); for the second, Dr. Butler (of Montevideo); for the third, Dr. Maissa (of Argentina) and Dr. Gonzalo Esguerra Gómez (of Colombia). There will probably be, also, a fourth subject for discussion: "Physical Therapy of Rheumatic Diseases Affecting the Joints."

There will be a large exhibition of roentgenograms referring to the subjects under discussion, as well as a scientific exhibit of apparatus and accessories.

Will it be possible for some of the North American radiologists to attend this Convention? If we may have the names of any such, official invitations will be extended them through the proper official channels, by the Argentine Minister of Foreign Affairs, and we will

have the honour of considering the official narrators as our guests during the period when the Congress takes place.

With kindest regards and best wishes, I am

Yours very truly,

José F. Merlo Gómez, President of
The Radiological Society of Argentina

According to the rules of the Convention official membership is limited to members of radiological societies (except for countries where no such society exists). The fee for membership is 20.00 Argentine pesos. Any official member may present a paper, provided it deals with one of the subjects announced for discussion.

If any member of the Radiological Society of North America finds it possible to attend this Convention, he should communicate with Dr. Donald S. Childs, Secretary of the Society, in order that his credentials may be forwarded to Doctor Gómez, President of the Convention. The period for enrollment expires sixty days before the opening session.

WAR CONFERENCE

The American Association of Industrial Physicians and Surgeons, the American Industrial Hygiene Association, and the National Conference of Governmental Hygienists are this year combining their annual meetings in a four-day "War Conference" at Rochester, New York, May 24–27, 1943. An invitation is extended to physicians and surgeons, hygienists, engineers, nurses, executives—all who are interested in the problems of industrial health and their solution—to attend as many of the sessions as possible. No registration fee is required.

In Memoriam

KENNETH JASTRAM HOLTZ, M.D.

Dr. Kenneth J. Holtz, of Seattle, Washington, died on Jan. 9, at the age of fifty-two. Doctor Holtz was a graduate of Jefferson Medical College, Philadelphia, and saw service in World War I. He was a member of the Radiological Society of North America and was Secretary-Treasurer of the Washington State Radiological Society.

Book Reviews

A Study of the Blood in Cancer, with Special Reference to the Needs of the Tumour Clinic. By O. Cameron Gruner, M.D. (Lond.). A monograph containing 100 pages with 39 figures. Published by Renouf Publishing Company, Montreal, 1942. Price $4.00.

This small text by O. Cameron Gruner is the result of his studies over many years of the changes occurring in the morphology of the blood in cancer. It represents a tremendous amount of work, but because of the detail required is unlikely to find application in the general laboratory.

A study of the blood in cancer is always worth while but whether one is justified in drawing the conclusions presented by Doctor Gruner will have to await the confirmation of his work by other observers. It seems unlikely that many hematologists would agree that what he terms endotheloid monocytes (p. 26) would be confused with leukoblasts or myelocytes.

Doctor Gruner's general method of classification of cells is as complex as that of Arneth, and this immediately detracts from the value of the procedure because of the time required in making the observations. The book will be of value, however, to those who are interested in research work related to cancer.

Industrial Radiology. By Ancel St. John and Herbert R. Isenburger. A volume of 298 pages. Second edition. Published in London by Chapman and Hall, Limited, and in New York by John Wiley & Sons, Inc. Price $4.00.

This book is intended primarily for those engaged in industrial radiography rather than the medical radiologist. It should be of interest, however, to the physician who occasionally may be called as a consultant in this work. The first portion is devoted to the historical and physical aspects of radiology. The latter portions describe the technic of making radiographs of various types of castings and welds. A chapter is also included on radiography with gamma rays of radium. In the appendix various charts and tables are given which should be of considerable value. A comprehensive bibliography is appended, and the book is well illustrated.

RADIOLOGICAL SOCIETIES OF NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate by sending information to Howard P. Doub, M.D., Editor, Henry Ford Hospital, Detroit, Mich.

UNITED STATES

Radiological Society of North America.—Secretary, D. S. Childs, M.D., 607 Medical Arts Building, Syracuse, N. Y.

American Roentgen Ray Society.—Secretary, Harold Dabney Kerr, M.D., Iowa City, Iowa.

American College of Radiology.—Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill.

Section on Radiology, American Medical Association—Secretary, J. T. Murphy, M.D., 421 Michigan St., Toledo, Ohio.

ARKANSAS

Arkansas Radiological Society.—Secretary-Treasurer, J. S. Wilson, M.D., Monticello. Meets every three months and annually at meeting of State Medical Society.

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, Joseph D. Coate, M.D., 434 Thirtieth St., Oakland.

Los Angeles County Medical Association, Radiological Section.—Secretary, Donald R. Laing, M.D., 65 N. Madison Ave., Pasadena. Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Secretary-Treasurer, L. Henry Garland, M.D., 450 Sutter St., San Francisco. Society meets annually during annual meeting of the California Medical Association.

San Francisco Radiological Society.—Secretary, Earl R. Miller, M.D., University of California Hospital. Meets monthly on third Thursday at 7:45 P.M., for the first six months at Toland Hall (University of California Medical School); second six months at Lane Hall (Stanford University School of Medicine).

COLORADO

Denver Radiological Club.—Secretary, Edward J. Meister, M.D., 366 Metropolitan Bldg. Meetings third Friday of each month at the Denver Athletic Club.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary-Treasurer, Max Climan, M.D., 242 Trumbull St., Hartford. Meetings bimonthly, on second Thursday. Place of meeting selected by Secretary.

FLORIDA

Florida Radiological Society.—Acting Secretary, Walter A. Weed, M.D., 204 Exchange Building, Orlando.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, James J. Clark, M.D., 478 Peachtree St., N. E., Atlanta. Meetings twice annually, in November and at the annual meeting of State Medical Association.

ILLINOIS

Chicago Roentgen Society.—Secretary, Warren W. Furey, M.D., 6844 S. Oglesby Ave. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Fay H. Squire, M.D., 1753 W. Congress St., Chicago.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, Harold C. Ochsner, M.D., Methodist Hospital, Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secretary-Treasurer, Sydney E. Johnson, M.D., Louisville City Hospital, Louisville. Meeting annually in Louisville, third Saturday afternoon in April.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., North Louisiana Sanitarium, Shreveport. Meets annually at same time as State Medical Society.

Shreveport Radiological Club.—Secretary-Treasurer, R. W. Cooper, 940 Margaret Place. Meetings monthly on the second Wednesday, at the offices of the various members.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

Michigan Association of Roentgenologists.—Secretary-Treasurer, E. M. Shebesta, M.D., 1429 David Whitney Bldg., Detroit. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—Secretary, John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

Radiological Society of Greater Kansas City.—Secretary, Arthur B. Smith, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—Secretary, Paul C. Schnoebelen, M.D., 462 N. Taylor Ave. Meets on fourth Wednesday of each month except June, July, August, and September, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—Secretary, F. L. Simonds, M.D., 1216 Medical Arts Bldg., Omaha. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society (Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island).—*Secretary,* Hugh F. Hare, M.D., Lahey Clinic, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, H. J. Perlberg, M.D., Trust Co. of New Jersey Bldg., Jersey City. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.—Secretary, William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, Leo Harrington, M.D., 880 Ocean Ave. Meetings held the fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Joseph S. Gianfranceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Ray Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Maurice Pomeranz, M.D., 1120 Park Ave., New York, N. Y.

Rochester Roentgen-ray Society.—Secretary, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meeting with State meeting in May, and meeting in October.

NORTH DAKOTA

North Dakota Radiological Society.—Secretary, L. A. Nash, M.D., St. John's Hospital, Fargo. Meetings by announcement.

OHIO

Ohio Radiological Society.—Secretary, J. E. McCarthy, M.D., 707 Race St., Cincinnati. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society.—Secretary-Treasurer, J. O. Newton, M.D., 13921 Terrace Road, East Cleveland. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Samuel Brown, M.D., 707 Race St. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport. The Society meets annually.

The Philadelphia Roentgen Ray Society.—Secretary, Robert P. Barden, M.D., 3400 Spruce St., Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

The Pittsburgh Roentgen Society.—Secretary-Treasurer, Reuben G. Alley, M.D., 4800 Friendship Ave., Pittsburgh, Pa. Meetings are held on the second Wednesday of each month at 4:30 P.M., from October to June, at the Pittsburgh Academy of Medicine, 322 N. Craig St.

ROCKY MOUNTAIN STATES

Rocky Mountain Radiological Society (North Dakota, South Dakota, Nebraska, Kansas, Texas, Wyoming, Montana, Colorado, Idaho, Utah, New Mexico).—*Secretary,* A. M. Popma, M.D., 220 North First St., Boise, Idaho.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer, Robert B. Taft, M.D., 103 Rutledge Ave., Charleston. Meeting in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—Secretary-Treasurer, Herman Klapproth M.D., Sherman.

VIRGINIA

Virginia Radiological Society.—Secretary E. Latané Flanagan, M.D., 215 Medical Arts Bldg., Richmond.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary-Treasurer, C. A. H. Fortier, M.D., 231 W. Wisconsin Ave., Milwaukee. Meets monthly on second Monday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russell F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

Canadian Association of Radiologists.—Honorary Secretary-Treasurer, A. D. Irvine, M.D., 540 Tegler Bldg., Edmonton, Alberta.

La Société Canadienne-Française d'Eléctrologie et de Radiologie Médicales.—General Secretary, Origène Dufresne, M.D., Institut du Radium, Montreal. Meetings are held the third Saturday of each month, generally at the Radium Institute, 4120 East Ontario Street, Montreal; sometimes, at homes of members.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meetings are held monthly.

ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

The Head and Neck

The Chest

The Digestive Tract

The Skeletal System

Gynecology and Obstetrics

The Genito-Urinary Tract

RADIOTHERAPY

ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Fractures of the Jaws: Should Teeth and Comminuted Bone Be Removed. D. G. Walker. Proc. Roy. Soc. Med. **35:** 663–682, August 1942.

Several factors must be considered in determining whether teeth and comminuted bone should be removed following fracture of the jaw. Thus there is a stronger case for preserving the front teeth in a young girl than in an elderly patient. Also, when other injuries occur in conjunction with jaw fractures, surgical dental treatment may have to be postponed or curtailed. These considerations, however, play an indirect role. The direct factors influencing treatment are enumerated as follows:

1. Exact relation of the teeth to the fracture. Carious and infected teeth not directly involved in line of fracture should be retained, as they may be an invaluable aid in splinting the jaw.

2. Condition of the teeth. Four aspects are of great importance here: the extent of the trauma, the degree of infection, the stage of development, and the stage of eruption of the teeth. Extraction of teeth in a badly comminuted fracture is much easier than in one of subperiosteal variety. In subperiosteal fractures, a better result is likely to be obtained by postponing extraction until the fracture is "sealed off." Conservative treatment is indicated in fractures involving developing and unerupted teeth.

3. Condition of the bone. Only in war injuries are alveolar fractures seen with much comminution and loss of bone and teeth. In such cases careful débridement should be carried out, with removal of damaged teeth and loose pieces of alveolar bone. If large portions of the alveolus are fractured, as few teeth as possible should be removed until sound union has taken place. The common type of fracture in civil life is an uncomminuted fracture of the mandible with a vertical or oblique fracture line. The general tendency toward conservatism in removal of comminuted bone in these cases is sound, provided comminution is not too extensive and there is no gross loss of bony tissue.

4. Roentgenographic findings. In this connection the degree of decalcification should be especially emphasized. Decalcification may be caused by lack of adequate immobilization and resulting traumatic hyperemia or by infection. In the presence of acute infection, sequence of treatment is important. The fracture should first be immobilized and the infection controlled by adequate drainage. Then, teeth that may be detrimental to the result can be removed.

5. Age of fracture when treatment is begun. The major problem in treating fractured jaws is prevention of infection and not the method of jaw immobilization. In removing bone or teeth, it is most important to choose exactly the right time. With bone it is a fixed principle that this be done either immediately after the injury or after it has separated. The problem is less easy to solve in case of teeth. In the early stages of fracture, trauma caused by extraction is often a grave danger. Later the best time depends upon degree of infection present.

This discussion is illustrated by numerous roentgenograms in all the required exposures, illustrating 38 cases of varied types of jaw fractures, with full explanatory notes. A careful study of these plates should be of great value to those interested in the field of dental surgery. STEPHEN N. TAGER, M.D.

THE CHEST

Bronchography: Use of a Modified Intranasal Method and a Movable Table. B. A. Dormer, J. Friedlander, and M. Gibson. J. Thoracic Surg. **12:** 35–43, October 1942.

The method described for the instillation of lipiodol into the lungs consists of injecting the oil into the anterior nares through a short rubber tube with an olive tip, the patient having been previously tested for iodine and cocaine sensitivity. A local anesthetic (2.5 per cent cocaine) is used in the nose, pharynx, and larynx, applied by means of a spray. The patient is in a semi-recumbent position and the tongue is pulled out during the injection. After the oil has been introduced, the patient is so placed that it will run into the part of the lung to be studied. In 250 cases the authors have had invariably good results.

The method appears to be the same as the supraglottic injection through the mouth except that the injection is made into the nose. A special table is described which makes it possible to tip the patient into any position. Fluoroscopy is not used.

HAROLD O. PETERSON, M.D.

Systematic Radiological Investigation of Populations. M. de Abreu. Radiologia **5:** 153–159, July-August 1942.

"Spectacular" medicine, with its pride in presenting only cases with complete sets of classic symptoms, has given way to the concept of "dynamic" medicine. Interest has shifted to the evolutionary stages of disease in an endeavor to detect cases before clinical manifestations become evident. The resulting more systematic examination methods have demonstrated the very high incidence of tuberculosis, and more particularly, cardiovascular disease, in persons totally unaware of their presence.

Clinical and bacteriological examinations are not dependable for the diagnosis of tuberculosis since in certain stages they give negative findings. Roentgenology, on the other hand, not only furnishes positive evidence of the present stage of the process, but also reveals its past history. In order to reach the great masses of the population, it has been necessary to introduce mass production methods, as it were. Roentgenology as a diagnostic procedure has become socialized.

The radiological images most fruitful of interpretation in tuberculosis are those caused by the initial infection or by reinfection. With respect to the latter we must differentiate between residual, potentially evolutionary, and frankly evolutionary forms. The distinction is important because of the great number of persons with latent or, to a certain extent, inactive tuberculous lesions which may flare up at any moment. Today we know that, far from being exceptional, these forms are numerous but also entirely curable. This fact broadens the definition of tuberculosis so as to include not only clinically active but also latent cases.

In Brazil, from which this paper comes, the cardiovascular diseases constitute a problem as grave as tuberculosis, if not graver. These diseases also have silent forms. Cardiovascular syphilis, for example, does not produce symptoms until late in its development. Investigations carried out since 1936 have shown an incidence of 4.83 per cent for all forms of circulatory disorders, exceeding that of tuberculosis in many urban areas in Brazil.

Systematic radiological examination at frequent intervals should be extended to increasingly larger groups of the population. Efforts since 1936 have borne many fruits, but very much remains to be done. Full success depends largely on a change in teaching methods in medical schools, whereby greater emphasis would be laid on the early recognition of disease. The layman, also, should give as much thought to the condition of his chest as he now may accord to other organs. ENRIQUE J. CERVANTES, M.D.

Why the Late Entry into the Sanatorium? V. A. Lookanoff. Dis. of Chest **8:** 305–315, October 1942.

In beginning, the author quotes statistics from various surveys showing that on admission to sanatoria, between 4 and 18 per cent of tuberculosis patients have minimal disease and between 76 and 82 per cent moderately or far advanced lesions. He discusses the methods of discovering tuberculosis but offers no new approach to diagnosis nor does he make clear "why the late entry into the sanatorium," except because of difficulties of diagnosis.

The following points are brought out. A negative physical examination or the absence of symptoms does not rule out tuberculosis. The x-ray diagnostically is 99 per cent efficient. Examination of contacts is from 15 to 30 times more effective than examination of the general population. A public health routine combining tuberculin tests, use of the fluoroscope, and roentgenography is recommended.

WM. H. GILLENTINE, M.D.

Report of an Epidemic of an Acute Respiratory Infection with Pneumonitis. A. F. Robertson, Jr. Virginia M. Monthly **69:** 542–544, October 1942.

During the past six years there have been numerous reports of an acute respiratory infection resembling in many ways influenza but presenting atypical areas of pulmonary consolidation, discovered largely by x-ray examination. These cases have occurred sporadically and in epidemics.

During October and November 1941, the author observed an epidemic of acute respiratory infection in a private preparatory school. Seventy-nine cases occurred in a student body of 450. Twenty-four of these cases fulfilled the requirements of so-called pneumonitis. In these the onset was similar to that in the milder cases except that the temperature range was higher and often reached a peak in two to five days. The cough was frequently distressing and the patient "appeared toxic." The temperature subsided by lysis, lasting for an average of ten days. The average period of hospitalization was 15.5 days.

Daily examinations of the chest were negative until the temperature had fallen to an average of 99.4°. At this time small and medium moist râles might be heard, usually over one of the lower lobes of the lung. Other physical signs were essentially negative, save for slight impairment of resonance over the affected areas in a few cases, and the presence of severe coughing. The sputum was scanty, tenacious, and difficult to raise. It was never rusty or blood-streaked. There was no pleural pain and no friction rubs were heard. No cyanosis or dyspnea was noted. No major complications occurred. The highest leukocyte count was 10,200; the average count 7,200. Tuberculin tests were negative.

X-ray studies were not made on all cases but 6 patients showed areas of infiltration extending out from the hilar region.

[The varied phases of these atypical pneumonias were covered in a Symposium presented before the Radiological Society of North America in December 1942 and published in the April 1943 issue of RADIOLOGY.]

JOHN E. WHITELEATHER, M.D.

Primary Coccidioidomycosis: Roentgenographic Study of 40 Cases. W. A. Winn and G. N. Johnson. Ann. Int. Med. **17:** 407–422, September 1942.

The authors have observed 40 cases of primary coccidioidomycosis throughout the period of clinical illness and until the roentgenographic pulmonary features have cleared, remained stable, or progressed. From their series of cases they have selected certain ones as illustrative of important roentgenographic aspects of primary coccidioidal infection. Roentgenograms of these are reproduced. The degree of pulmonary involvement varies considerably depending upon the amount of infection. A small nodular area of opacity may be all that is visible; on the other hand, there may be single or confluent areas of pneumonitis, usually in the pulmonary bases. In many instances the lesions appear to be predominantly exudative in character and clear fairly rapidly. Occasionally, they may leave a small amount of residual fibrosis. In the Negro and Filipino, perhaps owing to racial susceptibility, such primary exudative lesions have been observed to progress and result in early fatal dissemination of the disease. Pulmonary foci of primary coccidioidal infection show a tendency to assume the appearance of productive lesions, and then clear and decrease in size slowly and incompletely, leaving nodular densities that suggest caseation and that eventually may undergo calcification.

Cavity formation accompanying the early acute phase has been described. Such cavities, usually single, may close spontaneously, though they have a tendency to persist, despite regression of the other pulmonary lesions. They then assume a characteristic thin-walled and cyst-like appearance with little or no surrounding collateral reaction, and undergo little change in size, shape, or appearance over a period of several years. Such cavitation may be multiple. Localized bronchiectasis may also result from coccidioidal infection. Roentgenographic evidence of secondary mediastinal or hilar adenopathy is occasionally demonstrated. J. A. L. MCCULLOUGH, M.D.

Acute Putrid Abscess of the Lung: Hyperacute Variety. H. Neuhof and A. S. W. Touroff. J. Thoracic Surg. **12:** 98–106, October 1942.

In lung abscesses of the hyperacute variety the authors believe that early surgical treatment is imperative and feel there are no contraindications to operation. In earlier papers they have stated that

the roentgen appearance of the ordinary lung abscess is typical in only a minority of patients. In hyperacute cases, however, the films are usually characteristic. There is a large area of excavation with a fluid level. There is substantially more infiltration in the wall of the abscess; the lining of the cavity may be ragged, and the pleural reaction about the abscess is often intense and extensive.

The determination of the site of the pleural reaction is important, since the abscess must be approached through this region. When this is done a one-stage operation can be carried out and in these hyperacute cases a one-stage operation is essential. The authors have operated on 41 cases of hyperacute lung abscess with 3 deaths, and on 113 cases of acute lung abscess with one death.

HAROLD O. PETERSON, M.D.

Bronchial and Pulmonary Cancer. C. Wegelin. Schweiz. med. Wchnschr. **72:** 1053–1063, Sept. 26, 1942.

Clinical Aspect of Bronchial and Pulmonary Cancer. R. Staehelin. Ibid. 1063–1067.

Bronchial Cancer and Pulmonary Cancer. H. R. Schinz. Ibid. 1067–1070.

The Sept. 26 issue of *Schweizerische medizinische Wochenschrift* is devoted to papers presented at the meeting of the Swiss National League Against Cancer. The first three papers of the group, listed above, form a symposium on pulmonary cancer. The other papers deal with various aspects, mostly experimental, of the cancer problem.

Wegelin's paper covers the frequency, pathological anatomy, and cause of bronchial and pulmonary cancers. On the basis of 117 cases seen since 1900, it is concluded that there is a real age preference, most cases falling in the sixth decade, but that there is no evidence of an organized increase in the incidence over these years.

The gross pathology is lacking in uniformity, some authors distinguishing as many as seven different types of picture. The origin is frequently bronchial, and the right side is involved slightly more often than the left. Secondary changes due to necrosis or atelectasis are common. Direct invasion of neighboring organs may be a source of confusion as to the site of origin. Metastases may be widespread; the most frequent sites of lymphogenous metastases are the bronchial, mediastinal, and cervical nodes; of hematogenous metastases, the liver. Secondary lesions in the skeleton and many other organs were observed in the series.

The histologic picture is also rather confused. Undifferentiated carcinoma, squamous carcinoma, and cylindrical-cell carcinoma (adenocarcinoma) are discussed and illustrated. Etiologically, intrinsic and extrinsic factors are distinguished. Inheritance is not certainly proved in man. Actinic, mechanical, chemical, and infectious traumata may predispose to cancer. The Schneeberg lung cancers are cited as an example of the first type, and cancers due to inhalation of metallic dusts (arsenic, cobalt, nickel, bismuth) are mentioned. Roentgen irradiation may produce cancer-like epithelial changes in rabbits. These and other factors are discussed at length, but the statement that in most cases a combination of causes is the basis of the disease seems to indicate that these are only predisposing factors.

Staehelin, discussing the clinical aspects of the disease, begins with the statement that similar material can be found in medical texts. After mentioning the usual symptoms, he states that the roentgenographic picture is generally one of tumor plus atelectasis, edema, and secondary changes. Occasionally in upper lobe tumors one sees a characteristic picture, consisting of a solid shadow extending out from the hilus and sharply marked out from the collapsed upper lobe. The differential diagnosis is often troublesome, but bronchial and pulmonary cancer should be considered in the presence of: (1) cough with bloody sputum; (2) stubborn chest pain without demonstrable cause; (3) signs of tracheal or bronchial stenosis, or of a space-occupying lesion in the mediastinum; (4) stubborn pleural effusion, especially if bloody; (5) empyema or lung abcess without their concurrent findings; (6) cough with cachexia; (7) any indefinite disease of the respiratory organs; (8) evidence of other tumors which may metastasize.

Schinz briefly covers some of the same material on incidence and symptoms. He states that he does not favor puncture biopsy of the lung as a diagnostic method. Of 79 patients seen in his radiotherapeutic clinic from 1930 to 1940, 71 were male and 8 female. Only 1 carcinoma was seen arising in the alveolar epithelium, the rest being bronchial in origin. The site was the right upper lobe bronchus in 25, the left upper in 16, the exit of the upper bronchus in 12, the lower lobe bronchus in 11 (5 right, 6 left), and the right middle lobe bronchus in 2. Biopsy, done in 41 cases, gave a diagnosis of cornifying squamous carcinoma in 16, undifferentiated squamous carcinoma in 6, carcinoma solidum simplex in 5, small-cell carcinoma in 5, undifferentiated carcinoma in 8, and malignant tumor in 1. Four erroneous clinical diagnoses were made; in one the correct diagnosis was a fibroma of the left thoracic cavity, in one metastases from an ovarian carcinoma, in one bronchiectasis of the right upper lobe, and in one metastases from a carcinoma solidum simplex of the salivary gland. The rare superior pulmonary sulcus tumor (Pancoast) was seen but once.

The result of treatment is but rarely a cure. In only 3 patients treated was the life span over several years, and in none of these was histologic proof of the diagnosis obtained. Good palliation is often secured; in 42 per cent of Schinz's series a good initial result was obtained. But only 1 patient was alive and well after six years, and of those with distant metastases only 2 were alive and well for more than three but less than six months; 1 was alive with a recurrence more than twelve but less than eighteen months.

LEWIS G. JACOBS, M.D.

Carcinoma of the Bronchus. G. W. Holmes. New England J. Med. **227:** 503–508, Oct. 1, 1942.

This is a review of 158 proved cases of carcinoma of the bronchus previously reported and an additional 68 cases seen between Nov. 1, 1940, and March 1, 1942.

The incidence of bronchogenic carcinoma is about the same as for cancer of the rectum. It is a disease of men, rarely of women, of the "cancer age." The present operative mortality is about that of cancer of the stomach. Five-year surgical cures amount to about 4 to 6 per cent. Cures by irradiation are reported but there are no five-year cures in this group.

Early symptoms and signs are often lacking; usually

the symptoms are of advanced disease. Roentgen examination often gives the first clue to the condition, but definite diagnosis rests on bronchoscopy, thoracoscopy, or surgical exploration.

In the more recent group of 68 cases, 26 were epidermoid, 4 adenocarcinoma, 8 oat-cell carcinoma, 6 undifferentiated, and 14 unclassified.

Irradiation for palliation is sometimes effective, as in 2 of the reported cases, where the patients have been perfectly comfortable and apparently free of disease for eight months.

The roentgenologic appearance of carcinoma of the bronchus depends upon the location of the lesion, the type of tumor, the stage of the disease, and the complications. The tumor may develop centrally or peripherally. It may invade the lung tissue and form a large, round, dense mass, or it may be confined within the bronchus. Frequently a tumor is suspected from the obstruction it causes. If bronchial obstruction is complete only on expiration, emphysema will occur distal to the point of obstruction, and if this involves a large amount of lung, the mediastinum will shift away from the diseased side. If obstruction is total, a pneumonitis may develop in the distal area; or the parenchyma may become water-logged and infection with abscess formation may occur; or collapse of the distal lung may take place with mediastinal shift toward the affected side. In the far advanced case the picture is dominated by secondary manifestations.

Lymph node enlargement may be an early indication and should be looked for. Extension to the pleura frequently occurs when the tumor is in a small bronchus or near a septum. Phrenic nerve involvement may cause paralysis of a diaphragmatic leaf. Bone metastasis is not uncommon, and metastases in the brain, liver, adrenal glands, and mesenteric nodes are usual.

"The worth of roentgenologic examination is in the demonstration of a lesion consistent with carcinoma of the bronchus to the end that other more complicated diagnostic methods may be undertaken." Diagnosis should be confirmed by biopsy.

Surgery, if feasible, is to be preferred to irradiation. Irradiation may be expected to benefit patients with oat-cell or undifferentiated carcinoma without extension beyond the lymph nodes. The irradiation should be confined to the tumor tissue and about 3,000 to 5,000 r given in the tumor. Supervoltage irradiation is of distinct advantage.

JOHN B. MCANENY, M.D.

Bronchial Factor in Pulmonary Embolism. J. H. Jesser and G. de Takáts, Surgery **12:** 541–552, October 1942.

The authors report the third of a series of studies on pulmonary embolism (for their earlier reports see Surgery **6:** 339, 1939, and Arch. Surg. **42:** 1034, 1941, the latter abstracted in Radiology **38:** 120, 1942). The present experiments, carried out on dogs, concern the behavior of the bronchial tree.

For the roentgen studies iodochloral was injected directly into the trachea. A film was made five minutes later and embolism was then produced by injecting into the femoral vein 0.5 c.c. of a mixture of barium sulfate, iron perchloride, and normal salt solution. Seven groups of experiments were performed.

In *Series I*, in the bronchogram obtained five minutes after iodochloral injection, the trachea and larger bronchi were well visualized, including their finer branches. A second exposure, made immediately after the production of the embolus, showed that the opaque material had been squeezed into the terminal radicles, and the upper, middle, and lower main bronchi were invisible. A later film showed little change except for more bullous dilatation of the finer bronchi and patches of emphysema as a result of incomplete bronchial obstruction without infarction. Twelve experiments showed an identical pattern and in every instance the classical dyspnea and cyanosis of pulmonary embolism were present.

In *Series II*, no embolism was produced, but after visualization of the bronchi the trachea was clamped with forceps, causing severe dyspnea and cyanosis. Films obtained at the height of the respiratory distress, immediately after, and five minutes after release of the clamp, showed no change in the pattern of the bronchial tree, indicating that cyanosis and dyspnea were not responsible for the bronchial spasm seen in the previous series.

Series III comprised 4 experiments in which bilateral vagal section was performed. The appearance of the pattern interpreted as bronchospasm in the first series was uniformly prevented.

The animals in *Series IV* received 1/75 gr. of atropine intravenously before production of the embolism. This preserved the original bronchial pattern in 7 and failed to do so in 5 instances.

In *Series V*, 1/35 gr. of atropine was administered to 9 dogs; 6 of them obtained complete protection from bronchial spasm.

Seven dogs, constituting *Series VI*, were given 1/2 gr. papaverine. Some protection against bronchial spasm was obtained but this was less complete than with atropine.

In *Series VII* 1/2 gr. of papaverine and 1/75 gr. of atropine were administered to 9 dogs; 6 obtained fairly good protection.

Commenting on their observations, the authors state that the production of pulmonary embolism reveals in each instance a disappearance of the visible pattern of the main bronchi. This is due to bronchial spasm and is absent when the spasm is inhibited either by bilateral vagal section or by atropine in adequate dosage. The spasm is not due to hyperpnea or anoxemia, as mechanical obstruction to the trachea failed to produce scattering of the opaque substance into the final radicles. "As vagal stimulation produces bronchial constriction and surgical or pharmacologic block of the vagus abolishes the bronchial spasm, we have here another instance of reflex vagal impulses occurring during pulmonary embolism . . . . These reflexes have effects on the heart, on the pulmonary vascular bed, and on the bronchi, as shown in this report."

Discussing briefly the clinical applications of their observations, the authors state that the bronchial asthma of pulmonary embolism explains the frequent finding of areas of atelectasis in the films of patients suffering from embolism and suggest that some of the bronchial obstructions seen postoperatively may be of reflex nature, either originating from pulmonary emboli or possibly from intra-abdominal sources of irritation. [See the following abstract.]

J. E. WHITELEATHER, M.D.

Reflex Pulmonary Atelectasis. G. de Takáts, G. K. Fenn, and E. L. Jenkinson. J. A. M. A. **120:** 686–690, Oct. 31, 1942.

While there are many theories regarding the production of atelectasis, it is generally agreed that its essential cause is the obstruction of a bronchus with massive secretion. The suggestion has been made, however, that reflex nervous stimuli play a part in the initiation of bronchial obstruction.

Experimental evidence has been obtained [see preceding abstract] that pulmonary embolism artificially produced in dogs results in bronchospasm; that dyspnea does not of itself produce spasm, and that bilateral vagal section will inhibit its occurrence. Evidence has also accumulated to show that, associated with a reflex bronchoconstriction, an increased bronchial secretion occurs in the experimental animal. We have, then, the essential factors in the production of atelectasis, namely, obstruction and increased secretion. Of various intra-abdominal manipulations, traction of the cystic duct and pulling on the mesentery caused bronchospasm. Blunt injury to the chest wall, with or without rib fracture, also produces spasm of the bronchial tree. This can be prevented by the use of atropine.

Turning to the clinical aspects of the problem, the authors state that it has recently been pointed out that triangular infarcts are rare. This is borne out by their own investigations. It is their belief that, if the x-ray shadow that follows pulmonary embolism is due to reflex pulmonary atelectasis, then there is no good reason why the shadow should be triangular or funnel-shaped. Nor is there any reason, if the bronchial obstruction is due to reflex constriction and if this constriction can be relieved, why the patient should have a pneumonic episode. In a case of reflex atelectasis the decisive factor in the course of events is whether or not the bronchial obstruction is relieved. The relief of this bronchial obstruction should be one of the therapeutic aims.

Roentgenologically, in the first twenty-four hours nothing but the high-splinted diaphragm on the involved side may be evident in pulmonary embolism. In two or three days an area of consolidation appears, which may be pneumonic or atelectatic. Without clinical data the radiologist should not be expected to make a diagnosis of pulmonary embolism. Prompt disappearance of the area of consolidation points to atelectasis as the cause of the shadow. Regarding treatment of pulmonary embolism, the authors have data on 28 patients in whom an atropine-papaverine mixture was administered three times a day for three days. No massive atelectasis was seen in this group.

The second form of reflex atelectasis, namely, that occurring during surgical procedures, has now been reported several times. Some of the factors which may be responsible are insufficient pre-medication with atropine or scopolamine, too light an anesthesia, trauma at intubation, position of the patient, and possibly the parasympathetic action of cyclopropane.

Traumatic atelectasis deserves more recognition than it has received in the past. When contusions of the chest wall are thoroughly studied roentgenologically, some evidence of pulmonary change is observed in roughly three-fourths of the cases. It is suggested that there may be a nervous reflex involved in some of these bronchial obstructions, and that, instead of strapping the ribs, thus augmenting hypoventilation, they should be injected with procaine hydrochloride, in accordance with the practice of Harmon and his associates and ventilation should be encouraged.

The experimental findings of a reflex bronchoconstriction and bronchosecretion following pulmonary embolism fit in with the early clinical and roentgen observations in man. If the embolic atelectasis is originated by a nervous reflex, why could not the surgical or the traumatic atelectasis be initiated by the same mechanism. The authors' animal experiments indicate that this is at least a possibility.

Other causes of lobar collapse are, of course, well known. These are listed as peribronchial compression by glands, by tumors, or by swelling of the mucous lining around foreign bodies. That injections of iodized poppy seed oil may occasionally produce spasm followed by atelectasis in normal contractile bronchi was demonstrated in 1929 by Jacobaeus and his associates (see Brit. J. Radiol. **3:** 50, 1930. Abst. in RADIOLOGY **15:** 417, 1930).

CLARENCE E. WEAVER, M.D.

Spontaneous Hemopneumothorax: Report of Three Cases and Review of Literature. H. C. Hartzell. Ann. Int. Med. **17:** 496–510, September 1942.

Three cases of idiopathic hemopneumothorax are presented, and the literature is reviewed briefly. The condition is seen in young men without a history of previous lung disease. Clinically it presents in rapid sequence the onset of chest pain followed by dyspnea, anemia, and shock, associated with mediastinal displacement. The physical findings are those of hydropneumothorax, at times associated with confusing abdominal signs. The pathogenesis is not entirely clear, but some cases are known to develop when spontaneous pneumothorax resulting from rupture of an apical bulla is complicated by the tearing of pleural adhesions during the course of collapse of the lung. Treatment consists of rest, thoracentesis with or without the introduction of air, and possibly surgical intervention when necessitated by continued bleeding. The condition has no relation to active tuberculosis, and the prognosis, provided the patient survives the acute episode, is good. A comprehensive bibliography is appended. J. A. L. MCCULLOUGH, M.D.

Thrombosis of the Axillary Vein. I. Greenfield Ann. Int. Med. **17:** 732–738, October 1942.

Most authors agree that trauma of some type is responsible for thrombosis of the axillary vein. The patients are generally young, robust, and muscular, and engaged in heavy work. Swelling of the arm occurs immediately or several hours or days after sudden muscle strain or repeated muscular effort. The swelling spreads over the entire arm without rise in body or local temperature and without local inflammatory lesions. Venous collaterals develop on the affected arm and over the anterior portion of the chest. Venous pressure in the veins of the affected arm is increased. *Visualization* of the veins with an opaque medium reveals the presence of numerous collaterals, distended venous valves, and stasis of the dye in the vessels. Infra-red photography shows numerous superficial veins in the affected arm and over the chest.

The author presents a case in a 20-year-old female,

who was taken ill with an upper respiratory infection six weeks before she came under observation. No history of trauma was revealed. The pertinent negative findings were absence of a "Horner's collar," no tracheal tug or fixation, no broadening of the mediastinum, absence of tenderness above the right clavicle, and absence of a cervical rib. The positive findings conformed to the criteria for diagnosis given above. Accordingly, the author concludes that he has a case of idiopathic thrombosis of the axillary vein.

The prognosis as to life is good. Duration of disability varies from a few months to a year or more because of the persistence of edema.

Treatment indicated is complete rest, elevation of the extremity, and local application of heat. Rest and elevation should be maintained until edema has subsided and adequate collateral circulation has developed.

STEPHEN N. TAGER, M.D.

Normal Heart and Conditions Simulating Cardiac Disease. E. H. Stokes. M. J. Australia. **2:** 253–263, Sept. 19, 1942.

The author furnishes a comprehensive discussion of the normal heart with a chart of the cardiac findings in 15 normal medical students. In another chart are compiled conditions simulating cardiac disease in 45 selected patients and the cardiac findings in these cases.

In discussing x-ray examination of the heart the author reminds us that fluoroscopy should be done in the anteroposterior and the right and left oblique positions. This is important in determining the size and shape of the heart and the pulsations of the various chambers. Orthodiagraphy is done and a film is made when a permanent record is desired.

It is pointed out that variations of the heart at different ages must be kept in mind. For example, the right auricle undergoes rapid hypertrophy during the first six weeks of life.

The author emphasizes, also, the importance of the cardiothoracic ratio, which, it has been said, should not exceed 1:2. Variations of the ratio within the normal are to be expected. It may range from 1:4 in patients with long narrow chests to 1:1.9 in short, thick-set individuals. This was confirmed in the study of normal medical students. Ascites and abdominal tumor tend to cause elevation of the diaphragm and a relative transverse position of the heart.

DONALD R. LAING, M.D.

Contrast Visualization of the Heart and Great Vessels in Emphysema. M. L. Sussman, M. F. Steinberg, and A. Grishman. Am. J. Roentgenol. **47:** 368–376, March 1942.

Twenty-eight patients with emphysema of various types and grades were subjected to contrast visualization of the cardiac chambers and great vessels. The injections were made according to the technic previously described by Robb and Steinberg (Am. J. Roentgenol. **41:** 1, 1939) and the recording of the roentgen findings was carried out by various methods. In all cases visual observation and multiple photographs of the fluoroscopic screen made on 35-mm. film by the fluorographic method were employed. In many cases these were supplemented by moving pictures of the fluoroscopic screen, roentgen kymograms, and direct roentgenograms.

Particular attention was paid to the size of the right ventricle. In 12 cases this was definitely dilated and in 10 of these the septum was convex to the left. Twelve additional cases were classified as showing probable right ventricular dilatation and in these the septum convexity was to the right. In 4 cases the right ventricle and pulmonary artery appeared entirely normal; all of this last group were patients with chronic bronchitis.

Right axis deviation or interventricular block (Wilson's type) was constantly associated with abnormalities of the right cardiac chambers, but a normal electrocardiogram did not preclude the finding of right ventricular dilatation. In fact, in 8 cases a normal electrocardiogram was associated with definite convexity of the septum to the left, indicating right ventricular dilatation. In two cases of marked emphysema with chronic bronchitis of long duration, there was no right ventricular dilatation. No explanation is offered for this finding. In two other cases in which a normal right heart was found the clinical symptoms and normal vital capacity suggested extremely mild involvement. Coincidental left ventricular dilatation could be accounted for in many instances by essential hypertension or previous coronary thrombosis. In the remaining cases coronary sclerosis seemed to be the most likely explanation.

The findings in the 28 cases are presented in tabular form and one case, with postmortem findings, is reported in detail.

Evaluation of Heart Size Measurements. H. E. Ungerleider and R. Gubner. Am. Heart J. **24:** 494–510, October 1942.

The authors review physical, roentgenologic, and electrocardiographic methods of determining the heart size. They recommend use of the teleroentgenogram and provide a nomogram predicting transverse diameter of the heart from the height and weight of the patient. The cardio-thoracic ratio is not considered so reliable as the ratio between the heart rectangle and the lung rectangle, the rectangles being determined by multiplying the length by the breadth of the organs concerned. Inherent errors in measuring cardiac area and volume are discussed. A formula is given for predicting the transverse diameter of the aorta. Characteristic changes in the electrocardiogram suggesting ventricular hypertrophy are mentioned. This information should only be utilized by the experienced electrocardiographer. The article, critically read, contains much useful information.

WM. H. GILLENTINE, M.D.

Calcareous Aortic Stenosis in a Case of Dextrocardia With Situs Inversus. G. A. Abbott and H. I. Russek. Am. J. M. Sc. **204:** 516–521, October 1942.

Transposition of the viscera is an uncommon condition. Considerably more infrequent is the association of congenital dextrocardia with acquired lesions of the cardiovascular system. The acquired lesions reported have been mitral stenosis, hypertensive heart disease, coronary thrombosis, hypertensive and coronary artery disease, and syphilitic aortic stenosis and aortic insufficiency. The authors present a case of congenital dextrocardia complicated by calcareous aortic stenosis.

It is of interest to note that, in addition to dyspnea

and cough, the patient complained of aching pain in the right mammary region. His blood pressure was normal. A marked systolic thrill was present in the second and third intercostal spaces to the left of the sternum. A harsh systolic murmur was heard with maximum intensity in this area. The electrocardiogram showed unusually marked right axis deviation, slight elevation of the S-T segment, and upright T waves in Lead I. With reversal of the limb leads to correct for the dextrocardia, there was left axis deviation, slight depression of the S-T segment with inversion of the T wave in Lead I, indicating strain of the left ventricle. BENJAMIN COPLEMAN, M.D.

THE DIGESTIVE TRACT

Evidence of the Genesis of Peptic Ulcer in Man. S. Wolf and H. G. Wolff. J. A. M. A. **120:** 670–675, Oct. 31, 1942.

The authors found that day-to-day life situations which provoked certain patterns of emotional reaction induced hypersecretion in the stomach comparable to that resulting from prolonged absorption of histamine, vagus stimulation, and sham feeding in animals. Their studies were made on a man aged fifty-six who at the age of nine completely occluded his esophagus by drinking scalding hot clam chowder. Since that time he had fed himself through a gastric fistula 3.5 cm. in diameter, surgically produced shortly after the accident. He is employed in the authors' laboratory. Through the stoma there had protruded on the abdominal wall a collar of gastric mucosa essentially similar to that within the cavity of the stomach. Estimates of vascular changes were made by comparing changes in color in the gastric mucosa to a standard color scale. The output of acid by the parietal cells was estimated with reference to volume and acid concentration. In many of the experiments records of the stomach contractions were made by the familiar technic of inflating in the organ a balloon connected to a recording manometer. Careful note was made of the patient's mood and the content of his thoughts and preoccupations. These data were collected during the experiments as well as at daily interviews. The emotional reactions were then correlated with the various measurements of gastric function. The emotionally charged situations were not experimentally induced. Spontaneously occurring life situations, problems, and conflicts were utilized.

Every two or three hours there occurred in the stomach a transitory phase of hyperemia, hypersecretion, and vigorous contractions. These were spontaneous and lasted only twenty to thirty minutes. The stomach would then assume its former "basal" condition. At all times increased acid production was accompanied by hyperemia, and hyperemia always indicated increased acid production. Vigorous contractions, while they did not always accompany hyperemia, did not occur when the stomach was pale. Once, when the patient experienced intense fear, prompt and decided pallor occurred in his gastric mucosa, with an associated fall in the rate of acid production. When the fear disappeared the gastric mucosa regained its normal color. Sadness, dejection, and feelings of self-reproach were accompanied by taciturnity, lack of "energy," slowness of movement of the body generally, and by pallor of the gastric mucosa and decreased acidity and motor activity. Even the stomach's normal response to the ingestion of food was inhibited under these circumstances. In association with feelings of strong hostility and resentment on the part of the patient, and also with anxiety, his stomach became red and engorged and soon the folds were thick and turgid. Acid production was sharply accelerated and vigorous contractions began.

The degree and duration of the changes in gastric function were also roughly proportional to the intensity and duration of the emotional reaction. In the presence of hypermotility and hypersecretion the gastric mucous membrane not only became red but engorged and turgid as well. The susceptibility of the mucosa to injury resulting in hemorrhage was found to be greatly enhanced in this condition.

Small erosions and bleeding points which occurred from time to time were quickly covered with mucus and healed uneventfully in twenty-four hours or less. The protective powers of mucus have been shown to consist of three distinct mechanisms: First, it presents a continuous slippery surface to irritants. Second, by combining with and neutralizing the acid in immediate contact with it, it maintains the acidity of the stomach lining itself at a relatively low level. Irritants and the presence of acid in high concentration in the stomach accelerate the rate of production of mucus. The third protective property was invoked when the acid in the stomach exceeded the powers of this compensatory mechanism. The mucus precipitates and forms an insoluble, continuous, tough, membranous coating over the cells of the gastric mucosa, thus insulating them from chemical attack. In the duodenal cap the protection is far less elaborate. Thus the corrosive contents of the stomach can gain access to the base of a minor erosion.

The result of continued contact of gastric juice with a mucosal erosion was a sharp acceleration of acid secretion and concomitant hyperemia of the whole gastric mucosa. When an unprotected mucosal erosion was exposed to the digestive action of gastric juice additional tissue damage occurred, and ulceration with the appearance of chronic peptic ulcer resulted.

The authors conclude that the chain of events which begins with anxiety and conflict and associated overactivity of the stomach and ends with hemorrhage or perforation is that which is involved in the natural history of peptic ulcer in human beings.

CLARENCE E. WEAVER, M.D.

Chronic Gastric Ulcer in a Six-Year-Old Child. M. Kraemer and L. Townsend. Am. J. Digest. Dis. **9:** 338–340, October 1942.

"Ulcerations of the stomach and duodenum frequently resulting in death from hemorrhage or perforation are common immediately after birth, and in the first year of life." They are uncommon, however between the ages of two and twelve, only 26 cases having been reported in the literature in this age group. The authors describe a case of chronic gastric ulcer in a six-year-old child. The ulcer disappeared under treatment. JOSEPH T. DANZER, M.D.

Roentgen Diagnosis of Acute Intestinal Obstruction. M. D. Teitelbaum. New Orleans M. & S. J. **95:** 157–168, October 1942.

The case histories and roentgenograms of 61 patients were reviewed as a basis for this paper. It is clear

that the ready, accurate diagnosis of mechanical obstruction of the small bowel has three prerequisites: (1) the obstruction must be complete or nearly complete; (2) it must be sufficiently low so that the patient cannot, by vomiting, efficiently evacuate the bowel above the obstruction; (3) nothing which might interfere with the normal functioning of the bowel below the point of obstruction may be present.

The author's cases are broken up into groups. In *Group I* (24 patients) the typical findings of complete obstruction were present on the first films. In *Group II* (14 patients) obstruction was incomplete but sufficient for diagnosis. Discrepancy between the caliber of the proximal and distal loops was sufficient to permit a diagnosis of incomplete obstruction of the small intestine. In *Group III* (3 cases) the initial findings were inconclusive. Serial studies, *i.e.*, every two to four hours, were necessary in order to observe completion of obstruction. In *Group IV* (4 cases) the site of obstruction was too high for visualization on flat films. In *Group V* (16 cases) the degree of obstruction was insufficient for definite diagnosis. In 3 cases there was no distention of small or large bowel. In 13 cases, they were uniformly distended.

As regards localization of obstruction in the small intestine, the position of the distal distended loop may be depended on to indicate the segment of involved bowel in cases of complete obstruction of longer duration with adequate fluid-gas interchange. If the distended loops all lie in the upper abdomen, it may be assumed that the jejunum is obstructed; if in the lower, the ileum. When a diffuse gaseous distention of the intestinal tract is present and low mechanical obstruction is ruled out by visualization of a gas-filled rectum or by a barium enema, the only possible roentgen diagnosis is adynamic ileus.

A mixed form of paralytic and mechanical ileus, such as is produced by diverticulitis and intraperitoneal abscess particularly of the appendiceal region may closely simulate strangulation obstruction. The direct roentgen findings are of no differential value.

Barium enemas are, of course, of extreme importance in determination of mechanical and fecal obstruction, intussuception, and in primary carcinoma. This procedure is advised to determine the exact level and nature of the etiologic agent.

In conclusion, the roentgen diagnosis of obstruction depends upon the *visualization of distended intestinal loops*, which are outlined by their gaseous and liquid contents, and not upon the demonstration of gas and fluid in the bowel.

The absence of characteristic x-ray findings in some cases of obstruction with strangulation is disconcerting. Whenever there is any suspicion of the latter, a negative x-ray film should not be given much weight. Positive findings should be accepted as a stroke of good fortune and not a *sine qua non*. In general, however, there is a high index of correlation between roentgen and clinical findings in intestinal obstruction.

STEPHEN N. TAGER, M.D.

The Non-Functioning Gastro-Enteric Stoma: Diagnostic Study of 62 Surgically Demonstrated Cases. G. B. Eusterman, B. R. Kirklin, and C. G. Morlock Am. J. Digest. Dis. **9:** 313–317, October 1942.

A study of 62 surgically demonstrated cases was made by the authors. These were selected on the basis of a roentgenologic diagnosis of non-function of a gastro-enteric stoma.

It is important that the roentgenologist be informed that a gastro-enterostomy has been performed, as barium does not always pass through a stoma during the brief period of examination, although it may be functionally competent. A non-functioning stoma from a roentgenologic standpoint does not necessarily imply total gastric obstruction. It has also been found that a stoma that is closed at the time of roentgenologic examination may be open and uninvolved at the time of operation. This can be explained only by concluding that the obstruction is of a spastic nature which relaxes under a general anesthetic.

The usual routine of giving a few swallows of barium and examining the rugae and stoma should be done; larger amounts of barium are then given. It is seldom safe to base a definite diagnosis of non-functioning stoma on the results of any single examination.

The patients studied were divided into three groups on the basis of symptomatology. *Group 1* accounted for 77 per cent of the series. Symptoms were typical of ulcerative or anastomotic inflammatory lesions, such as extension of pain to the back and hypogastric area, and a high titre of gastric content. A subacute perforating ulcer was usually found at operation. *Group 2* comprised patients whose symptoms were not as severe and were more inclined to be localized. These cases showed a marginal ulcer or gastrojejunitis. In *Group 3* symptoms of obstruction were present, there was usually achlorhydria, and at operation a mechanical obstruction of the stoma was found, as a rule.

JOSEPH T. DANZER, M.D.

Roentgenological Study of the Postoperative Abdomen. J. Levitin and L. M. Trauner. Surg., Gynec. & Obst. **75:** 510–514, October 1942.

Three groups of cases were examined by means of x-ray films of the abdomen: (1) 20 unselected postoperative cases; (2) 65 patients who entered the hospital with abdominal distention and suspected bowel obstruction; (3) 22 selected cases of postoperative distention.

From the studies it is concluded that the x-ray findings in abdominal distention are significant and important in differentiating paralytic ileus from mechanical obstruction. The distention occurring twenty-four to ninety-six hours after operation is usually paralytic ileus. It is not the result of any one type of anesthesia.

Mechanical block may exist without clinical evidence. Conversely, severe lesions of the bowel may exist with symptoms but without x-ray evidence, especially when loops of bowel become strangulated.

Obstruction of the colon with back pressure into the small bowel, producing distention of both, presents a confusing x-ray appearance. Unless there is an abrupt end to the gas column in the colon, a barium enema should be given to differentiate between paralytic ileus and mechanical obstruction.

Transient postoperative obstruction is often due to thin fibrin bands which are easily broken. In these cases relief may be obtained by use of the Miller-Abbott tube. The tube is of more value in these cases than in postoperative cases because the probable duration of the obstruction and condition of the bowel are better known.

IVAN J. MILLER, M.D.

THE PANCREAS

Clinical Features of Pancreatic Lithiasis. Report of Two Cases. R. E. Moss and E. D. Freis. New England J. Med. **227:** 590–594, Oct. 15, 1942.

The literature on pancreatic lithiasis is reviewed and two complete case histories with laboratory findings are presented. These cases were studied with the aid of the pancreatic stimulants secretin and mecholyl.

The origin of pancreatic stones is not clear but chronic infection with deposition of calcium salts is believed to be the sequence. Pancreatitis, cholecystitis, and cholelithiasis are regarded as predisposing factors.

The clinical diagnosis is difficult because the condition is not considered. There are upper abdominal pain or colic, often referred to the left side, nausea, and vomiting. Attacks may be induced by fatty foods or more frequently by alcoholic excesses. Fatty diarrhea is most characteristic but is present in only about half the reported cases. Hepatic enlargement occurs. Diabetes mellitus, actual or latent, may be present. Icterus may occur. A flat film of the abdomen may demonstrate the stones.

In the two reported cases mecholyl was used to study the pancreatic enzyme production. Two separate studies were made on each patient. The amylase and lipase were found in a low normal range in both cases, but increased after stimulation with mecholyl, indicating that some pancreatic damage had been done. The incidence of diabetes or latent diabetes is greater in patients with pancreatic stones of long duration.

Operative removal of stones with recent improvements in technic has resulted in some cures.

JOHN B. MCANENY, M D.

THE BILIARY TRACT

Treatment of Common Duct Stone Missed at Operation. H. B. Morton. Surgery **12:** 591–598, October 1942.

Surgeons admit freely the high incidence of stones left in the biliary tree following surgery undertaken for their removal. The embarrassing facts associated with this situation are a continuance of dyspepsia, pain, jaundice, chills and fever, and the high mortality rate associated with a secondary search for these stones. These secondary operations are so undesirable that any less difficult or hazardous procedure of dealing with the overlooked common duct stone is acceptable.

Several reports have been made describing the dissolution of stones in the common duct by the injection of ethyl ether through a drainage tube in the duct. The author reports two cases. In one the patient was first observed with symptoms of common duct obstruction. The duct was opened and a probe passed easily into the duodenum. No stones were discovered. The gallbladder was removed and a T tube was placed in the common duct. Following the operation the patient continued to have symptoms and a cholangiogram on the 34th postoperative day demonstrated a calculus at the distal end of the common duct. A mixture of one-third ethyl alcohol and two-thirds ethyl ether in amounts of 5 c.c. was injected daily into the T tube, for five days. The following day a cholangiogram failed to show any evidence of stone and later cholangiographic study showed a prompt free flow of the medium into the duodenum. The patient has remained well since.

The second patient entered the hospital because of right upper quadrant pain, jaundice, chills, and fever. There was a history of dyspepsia of the gallbladder type for ten years, with mild recurrent attacks. After considerable preparatory treatment the patient was operated on and the gallbladder was found to be small, thickened, and injected, with a small gangrenous area at the fundus. It was filled with stones of various sizes. The common duct was opened and a number of stones removed; a probe passed easily into the duodenum. Cholangiograms on the 16th and 26th days revealed obstruction of the common duct believed to be due to a stone in the ampulla of Vater. Six daily injections of a mixture of 4 c.c. of ether and 2 c.c. of ethyl alcohol were made into the T tube. After the fourth the stools became dark brown and the epigastric distress disappeared. A cholangiogram showed complete disappearance of the obstructive shadow in the ampulla.

J. E. WHITELEATHER, M.D.

THE SKELETAL SYSTEM

Developmental Age of the Newborn and the Development of the Epiphyses. J. H. Müller and J. Balbi. Schweiz. med. Wchnschr. **72:** 1013–1015, Sept. 12, 1942.

The significance of the development of the epiphyses for determining the developmental age of the newborn was studied by roentgen examination of 50 normal and 25 post-term infants. It appears that the average relative number and size of the epiphyses are increased in over-gestation; but the epiphyses develop in a very irregular manner from case to case, so that from these findings alone no certain conclusion in the individual infant can be drawn relative to over-gestation. This fact stands in contradiction to the assertions of Stampfel and Tscherne (Ztschr. f. Geburtsh. u. Gynäk. **119:** 31, 1939) that a tibial epiphysis at least 7 mm. in diameter and a medial epiphysis of the humerus at least 5 mm. in diameter can be taken as certain signs of over-gestation. The roentgenologic demonstration of the state of the epiphyses is, it is true, within limits a help in determining over-gestation, but only in conjunction with other clinical data.

Furthermore, on the basis of observations made on monozygotic twins, the evidence points to the belief that factors of nourishment can influence the development of epiphyses. This in turn points to the probability of effects of constitutional and hormonal factors, both from mother and child.

LEWIS G. JACOBS, M.D.

Tabetic Arthropathies. A. Steindler, L. A. Williams, and J. Puig-Guri. Urol. & Cutan. Rev. **46:** 633–649, October 1942.

Charcot believed that the trophic joint lesions of tabes were due to changes in the cord and the posterior roots. More recently Eloesser, having produced Charcot changes in cats by cutting the posterior nerve roots, concluded that it is trauma, combined with analgesia —and consequent lack of warning pain—which is responsible for most tabetic lesions of the bones and joints.

The authors analyze a series of 134 cases with a total of 214 Charcot joints. In only 57 of these cases was

there a definite picture of tabes. Thus, of 106 cases, 30 per cent gave a negative serological test; only 82.5 per cent (62 observations) gave a positive Romberg sign and 80 per cent (99 observations) the Argyll-Robertson sign. The patellar reflex was absent in 82 per cent of 112 cases and only 9 patients complained of paresthesia and numbness of the limbs. Lancinating pains, apart from pain about the joint, were present in only 30 cases.

Symmetrical joint involvement was found in only 23 of the authors' cases. Seventy-nine per cent of his patients were males; 71 per cent were between the ages of forty and sixty. Fifty-nine cases had a sudden onset following fracture or other injury.

The local findings were painless swelling and effusion; pain on weight-bearing (in a minority of cases); abnormal mobility, especially of knee and ankle joints, which are most frequently involved; pathological fractures, associated with extensive osteoporosis, vascularization of the compacta, diminution of elastic fibers, and frequent Howship's lacunae; sensory skin changes and redness (infrequent); joint deformities.

Cardinal roentgen findings in Charcot joints are sclerosis, fragmentation, absorption, free body formation, exostosis and new bone formation, extra-articular ossifications, osteoporosis, pathological fractures, dislocations, and effusions.

The gross pathological findings are in accord with the roentgen observations. There is destruction of large masses of bone adjacent to the articular surfaces, and degeneration of synovia and ligaments is seen. Bony ankylosis is never found.

Following this general discussion the authors consider the special localizations, considering in some detail the changes in the skull, the upper and lower extremities, and the spine.

Treatment is in general conservative, though good operative results have been obtained in selected cases.

MAURICE D. SACHS, M.D.

Post-Traumatic Painful Osteoporosis. A Clinical and Roentgenological Entity. L. G. Herrmann, H. G. Reineke, and J. A. Caldwell. Am. J. Roentgenol. **47:** 353–361, March 1942.

Post-traumatic osteoporosis as a major cause for prolonged loss of function or severe aching pain following injury to an extremity—either trivial or severe—is not generally recognized. The early recognition of the condition is essential if the period of disability is to be favorably influenced by active therapy and permanent injurious effects are to be forestalled. Since the osseous changes are characteristic, the roentgenologist is the first to have the opportunity of making a diagnosis.

Clinically post-traumatic osteoporosis is characterized by partial loss of motor function of the affected part, vasomotor and trophic changes of varying degree in the extremity involved, and mild to severe aching pain, which is not relieved by immobilization. The disturbances of function are always more extensive than can be explained on the basis of the trauma alone, and the pain in the extremity is greatly out of proportion to the local signs of injury to the tissues.

The short bones of the hands and feet are most frequently affected. Next in order of frequency are the epiphyses of the metatarsals, metacarpals, and phalanges; then the epiphyses of the long bones. The diaphyses of the long bones are rarely involved.

Roentgenologically, two main forms have been recognized—an acute and chronic—representing different stages in the evolution of the disease. The authors describe typical cases of osteoporosis of the short bones, especially the carpal and tarsal bones, as showing three stages: the onset, the height of the disease, and reorganization.

In the *period of onset* there is a general mottled appearance of the bones, though their outlines are still easily discernible. The rarefaction continues to become more marked and more extensive and the bones soon become uniformly permeable to the roentgen rays.

The stage of diffuse and marked demineralization marks the *height of the disease*. The absorption of the bone seems to spread to involve the heads of the metacarpals or metatarsals, then the phalanges, and finally the adjoining ends of the radius and ulna or the tibia and fibula as the case may be. The cortex of the bones has become thinned and shows longitudinal streaks. In the region of the carpal and tarsal bones this thinning of the cortex results in the disappearance of the limits of the bones and thus transforms the entire area into a homogeneous mass which is very permeable to the roentgen rays. It is at this stage that a diagnosis of tuberculous osteo-arthritis is frequently made.

During the *period of reconstruction* there is a slow reappearance of the calcium in the bones, though complete recalcification seldom takes place. In roentgenograms taken during this stage the limits of the small bones have again become visible and the longitudinal lamellae have become thickened. Complete anatomical restoration of the density of the bone is not necessary for complete symptomatic relief.

While spontaneous healing may occur, it is long delayed and ankylosis may result, producing permanent disability. The authors have found that the course can be greatly shortened and most of the serious complications avoided if the disease is recognized in the acute phase and treated by thorough denudation of the main artery to the affected extremity (periarterial sympathectomy). They have previously reported a series of 34 cases thus treated with prompt relief (Am. J. Surg. **51:** 630, 1941).

Post-Traumatic Para-Articular Ossification of the Knee Joint (Pellegrini Stieda's Disease). J. Kulowski. Am. J. Roentgenol. **47:** 392–404, March 1942.

Post-traumatic ossification in the region of the medial femoral condyle was described by Pellegrini in 1905 and by Stieda in 1908 and is known therefore as Pellegrini-Stieda's disease. While Pellegrini in 1938 collected 767 cases from the literature, the author was able to find only about 60 cases reported in English. Twenty of the latter for which data were available are summarized in a table and 11 new cases are reported.

Three theories are advanced to explain the development of the lesion: separation of a bony fragment; periosteal ossification; calcification of the soft parts with subsequent ossification (metaplasia). Pellegrini in his original report attributed the ossification to two distinct and combined processes: namely, periosteal proliferation and direct metaplasia of the ligamentous structure of the medial collateral ligament. This mechanism explains the occasional bilaterality of the lesion, its wide variation in structure, shape, and anatomical relationship to the medial femoral condyle,

its evolution and occasional spontaneous regression, its recurrence after premature surgical excision, the incubation period or interval necessary for its development after trauma, and the usual presence of a free radiant space interposed between the shadow and the free margin of the medial epicondyle. Microscopic studies support the hypothesis of metaplasia of the affected ligamentous structures, but other mechanisms may play a role in some cases.

Th clinical symptoms are those common to knee joint injuries. The final diagnosis rests on the roentgen findings, and repeated roentgen examination is indicated in cases in which persistent pain and limitation of movement cannot be explained on the basis of the primary injury. "Ordinarily the shadow on the roentgenogram is characteristic in size and shape. It is usually directed vertically or slightly obliquely and may be crescent, elongated, vermiform, triangular, fusiform, island, sequestrum, fragmented or spicule. Depending upon its relative position, it may be proximal, central, distal or combined. Characteristically there is a clear radiant space of varying degree between the shadow and the femoral condyle."

Depending upon the stage of development, two main types are recognized: the evolutive and stabilized forms. The former appears as an active, more or less hazy or fuzzy variegated opacification of the adjacent connective tissue. In the latter there is a well defined, dense, sharply outlined calcific or ossified shadow which forms a residual covering over the medial femoral condyle.

Spontaneous healing may occur. Excision is indicated when the ossification provokes marked disturbances but should be done only after the process has reached a so-called static state of maturity. It may then be considered to be a true foreign body which can safely be removed as such. Roentgen therapy has been advocated, particularly in recent cases.

Some notes on the medico-legal aspects are appended.

Osteopoikilosis Associated with Bronchogenic Carcinoma and Adenocarcinoma of the Stomach. R. J. Ritterhoff, and D. Oscherwitz. Am. J. Roentgenol. **48:** 341–346, September 1942.

Osteopoikilosis, a rare familial anomaly which affects most bones except the skull, is usually characterized by multiple areas of bony condensation in the epiphyses and metaphyses. Its association with carcinoma has not previously been reported. A case is described which showed this condition involving practically all the bones, as well as bronchogenic carcinoma and adenocarcinoma of the stomach. Autopsy revealed the osteopoikilosis simply as an incidental finding and not related to the malignant lesions.

S. M. ATKINS, M.D.

Roentgen Findings in Increased Lead Absorption Due to Retained Projectiles. H. R. Senturia. Am. J. Roentgenol. **47:** 381–391, March 1942.

The author reviews the rather scanty literature on lead poisoning from projectiles retained in the body over a long period and includes reports of the only 6 cases which he was able to find in which roentgenograms were reproduced. He adds 2 cases of his own. A critical study of these cases shows that certain changes occur in the roentgen apppearance of the retained missile which indicate the occurrence of lead absorption leading to chronic poisoning. Briefly the findings consist in fragmentation and disintegration of the missile and apparent infiltration of lead particles throughout the adjacent tissues. Whereas the bullet originally is well defined and sharply delimited, the changes which occur result in a diffuse disintegration of the main body of the projectile into numerous smaller particles, or into homogeneous metallic diffusion which may be rather sharply encapsulated from the surrounding tissues, or more likely infiltrates the surrounding tissues along the muscle, tendon, and fascial planes. The roentgen demonstration of such a transformation does not always coincide with a clinical picture of lead poisoning. It does, however, serve to indicate that absorption in sufficiently large quantities is a potential danger. These signs of saturation of the tissues with lead have been confirmed by analyses of specimens removed at operation and autopsy.

Both the nature of the projectile and the site of lodgment are to be taken into account in the consideration of possible lead poisoning. Infantry shot and shrapnel consisting largely of lead are more liable to disintegration and absorption than grenade fragments or aerial bomb splinters, which consist mainly of steel. Projectiles lodged in bone adjacent to an active joint have shown these changes more consistently than those situated elsewhere in the body.

Bone Infarcts. S. C. Kahlstrom. Am. J. Roentgenol. **47:** 405–416, March 1942.

Five cases of multiple bone infarction are reported, only one of which occurred in a caisson worker. None of the other patients had been exposed to compressed air.

The roentgenologic features are characteristic, consisting in well defined, often symmetrical mottled areas of increased density involving the medullary portions of the diaphyses, sometimes extending into the epiphyses. Involvement of the non-articular cortex is infrequent. The size varies from mere flecks to several decimeters. The larger lesions are often separated from the normal bone by a narow zone of calcification, and frequently contain cystic areas with surrounding calcification. The necrotic bone may become completely calcified, leaving a homogeneous, dense, nonreticulation defect.

In 3 of the 4 non-occupational cases arteriosclerosis was present and the author suggests that it may eventually be established that bone infarcts result from arteriosclerosis as well as from caisson disease. Phemister (Arch. Surg. **41:** 436, 1940) and Chandler (Am. J. Roentgenol. **44:** 90, 1940) have reported cases with arteriosclerotic changes.

The Laminagraph as an Aid in the Treatment of Chronic Osteomyelitis. A. de F. Smith and L. E. Miller. Surg., Gynec. & Obst. **75:** 507–509, October 1942.

Accurate localization of the abscesses in chronic osteomyelitis is often difficult, since in ordinary x-ray films these may be hidden by thickened and sclerotic bone. Sinus tracts leading to these abscesses are frequently long and tortuous and hard to demonstrate. Blind surgical efforts to locate the cavity are usually unsuccessful.

Laminagraphic studies have proved useful in re-

vealing cavities not visible on ordinary x-ray examinations. They afford increased bone detail and better localization of the abscess both as to site and level. Their use may prevent exploration for a single abscess when more may be present. Lipiodol injection of draining sinuses for roentgen examination is suggested.

Three cases are presented and illustrative roentgenograms and laminagrams are reproduced.

IVAN J. MILLER, M.D.

Patella Cubiti: Report of Four Cases. J. E. Habbe. Am. J. Roentgenol. **48:** 513–526, October 1942.

The author gives a thorough review of the literature dealing with patella cubiti. He would not include as true patella cubiti similar conditions which are obviously the result of trauma in adult life.

That the typical true condition of patella cubiti, a decided rarity, as indicated by the lack of reports in the American roentgenologic literature, may be either of developmental anomaly origin or of traumatic origin still appears likely. A third possible explanation of the etiology is an "epiphysitis" of the olecranon, similar to so-called epiphysitis of the lumbar vertebrae resulting in ununited rim bands along the margins of one or several lumbar vertebral bodies. In the vertebral bodies showing these changes there has been almost universal absence of any history of injury in childhood. Traumatic separation of the epiphysis for the vertebral body margins is, furthermore, extremely rare. It is further pointed out that these secondary epiphyses for the vertebral body margins and the epiphysis for the olecranon undergo initial ossification at about the same age (nine to twelve) and the former, like the latter, normally unite with the primary center between the fifteenth and eighteenth years. Further, the primary center or main portion of the bone plus the anomaly or ununited epiphysis, together constitute a larger or longer structure than in the normal opposite ulna or adjacent vertebra. This is not true in epiphyseal fractures.

Each of the author's cases occurred as a unilateral abnormality. In one case there can be little doubt that trauma was the chief if not the only etiologic factor. In this instance the abnormality was found in a boy of fifteen, about five weeks after trauma, and the condition was followed for a period of six months, or until a relatively mature state of patella cubiti had occurred. In another case there was a definite history of trauma to the right elbow at the age of fourteen years. One would be inclined to suppose in this case that an avulsion of the olecranon epiphysis occurred together with periosteal stripping on the proximal diaphysis of the shaft by the mechanism of muscle pull, which was then followed by closure of the epiphysis and new bone formation. When the patient was seen at the age of twenty-two a condition of patella cubiti was found. Another patient, aged thirty-three, gave no past history of elbow trauma. In this instance, there were minor developmental disturbances, affecting the epiphyses for the body margins of the eleventh dorsal and third and fifth lumbar vertebrae.

In patella cubiti any trauma significant to the development of the condition must be one occurring in childhood or adolescence. Hence trauma occurring in an adult employee who shows such an abnormality is not a causative factor in its appearance and the misinterpretation of "fracture" or "pathological fracture" should not be made.

CLARENCE E. WEAVER, M.D.

Improved Localization and Treatment of Ruptured Intervertebral Disks. W. E. Dandy. J. A. M. A. **120:** 605–607, Oct. 24, 1942.

In the diagnosis of a ruptured intervertebral disk, the author places emphasis on the patient's story of low backache plus sciatica, occurring in attacks, usually after a relatively trivial injury, as in lifting or bending, or a strain. During the acute stages the pain in the back and the sciatica are usually intensified by coughing and sneezing. The only really valuable objective finding is a diminution or loss of an achilles reflex, and this occurs in only about half the cases. The diagnosis can be made by the clinical symptoms alone. Injection of contrast media into the spine is considered unnecessary.

So-called concealed disks cause the same signs and symptoms as protruding disks and the treatment is the same. All of these would be missed by intraspinal injection of a contrast medium and they now outnumber the protruding disks 3 to 2. It is the failure to detect the concealed disks at operation that has cast so much discredit on this field. Other lesions which may cause fairly similar symptoms are: tumors of the cauda equina, congenitally defective fifth lumbar vertebra with destruction of the articular processes, and spondylolisthesis. Carcinoma invading the low retroperitoneal spaces offers a fourth possibility of error.

Ninety-six per cent of all ruptured disks occur in the lumbar region, and 98 per cent of these are at the fourth and fifth lumbar vertebrae. The occasional case occurring higher in the spine gives symptoms suggesting a lesion higher than the routine levels. With the standard pain in the lower lumbar region and down the hips and back of one or both legs, the affected disk is nearly always at the fourth or fifth lumbar vertebra and it has been necessary to explore only one or both of these disks to find it. Frequently there is a lead, such as a reduced or absent achilles reflex, which points to the fifth, although this may also exist with involvement of the fourth. Also a narrowed disk may be evident in the roentgenogram.

When the unilateral exposure of the spine has been made, the incision uncovers both the fourth and fifth laminae. A periosteal elevator pushes the spines of the fourth and fifth spinous processes downward, *i.e.*, caudally, and determines the mobility of each vertebra. The disk will be where the greater movement is shown. The defective disk has weakened the spinal column locally and this in turn causes mobility. It is this free play at the disk that is responsible for the intensification of the pain by coughing and sneezing. Search should be made for more than one disk, as multiplicity is not uncommon.

The author insists that the interior of the disk must be treated by breaking up the contents with the forceps. It is not sufficient to remove protruding cartilage and as much more as can be pulled out of the depths of the necrotic interior of the disk. It is probably better to remove enough of the lining cartilage to bare the bone and permit granulations to fill the cavity. It is felt that fusion operations are inadvisable and unnecessary.

In the presence of spondylolisthesis or a defective fifth lumbar vertebra a defective disk may or may not be present. With such findings, preparation for fusion is made at the time of the operation and is carried out only when there is no disk.

There are very few sciaticas with low backache that are not due to defective disks. Remissions in symptoms are the rule, but throughout life the patient is subject to repeated attacks following slight strains on the spinal column. This is one of the most common ailments and one of the most debilitating, one of the easiest to diagnose and to cure permanently and with no risk. Delay in operation only means more suffering and subsequent attacks.

CLARENCE E. WEAVER, M.D.

Low Back Pain Resulting from Arthritis and Subluxations of the Apophyseal Joints and Fractures of the Articular Facets of the Lumbar Spine. W. G. Scott. Am. J. Roentgenol. **48:** 491–509, October 1942.

In the routine study of patients with low back pain roentgenograms should be made in the anteroposterior, lateral, and right and left posterior oblique positions. These may be made on four 10 × 12-inch films. The oblique views are made at an angle usually somewhere between 30 degrees and 45 degrees. The apophyseal joints, which are best shown in the oblique views, are true diarthrodial joints and are subject to the same types of disorders and diseases. The inferior and superior facets of adjacent vertebrae form the posterior border of the intervertebral foramen through which the nerves entering and leaving the spinal cord pass. This is an important anatomical relationship. The oblique position also provides a view of the entire lamina and the pars interarticularis. The lamina of the opposite side is seen in cross-section.

The normal variations of the facets and apophyseal joints include: variations in size and shape; variations in the degree of obliquity of the articular surfaces; variations in the width of the joint spaces; variations in the vertical alignment of the facets. These variations may occur from vertebra to vertebra in the same person. The articular surface of the superior facets of the lumbar vertebrae is concave, and in certain instances sufficiently curved so that it is impossible for the roentgen rays to pass through the joint space. This may lead to an erroneous interpretation of a narrowed or obliterated joint space. Taylor (J. A. M. A. **113:** 463, 1939) recently demonstrated that the direction in which the facets face is an important factor in maintaining the stability of the lumbar spine, particularly the lumbosacral joint.

Hypertrophic irregularities about the articular margins of the facets occur frequently in elderly people. Extreme hyperflexion or extension may cause overriding of the facets and damage to the articular cartilage and joint capsule, causing hemorrhage, edema, and swelling of the joint with resultant pain. The most common type of arthritis that can be demonstrated in the apophyseal joints is so-called rhizomelic spondylitis of the Marie-Strümpell type. The joint space is obliterated. The roentgen diagnosis of a localized, suppurative arthritis involving one or two of the apophyseal joints is quite difficult to make because of the normal variations which occur in these joints. The author reports but one case in which this diagnosis was made.

Subluxations of the apophyseal joints are not common, but occur sufficiently often to warrant greater attention than is customarily given them. Such a roentgen diagnosis can be made only in the presence of a narrowed intervertebral disk and an impingement with erosion of the ends of the facets on the lamina and pedicle of the adjacent vertebra. The pressure and movement of the facets against these structures eventually produce erosion or sclerosis or, in most instances, both. This causes pain. Pain may also be due to tension upon the capsular ligaments or encroachment of the facets on the lumen of the intervertebral foramen. The presence of a complicating posterior protrusion of the intervertebral disk should be ruled out.

Fractures of the articular facets are not as common (about one-eighth as common) as compression fractures of the lumbar vertebrae. They usually result from a direct violent blow to the back. Sudden hyperextension of the back and severe twisting may also result in fractures of the articular facets. Fractures must not be confused with congenital anomalies. One such anomaly is the presence of persistent centers of ossification that occur usually below the tips of the inferior articular processes of the lumbar vertebrae. They are usually bilateral. The fissures between the facets and the accessory ossicles are smooth and sharply demarcated by a white cortical line. The borders of fractures are usually ragged and irregular. The second congenital anomaly that must be distinguished from fractures is the congenital cleft in the lamina of the vertebrae. These are the precursors of practically all cases of spondylolisthesis. The margins of the clefts are smooth, clear-cut, and free from evidence of callus. They are usually bilateral. The oblique views often demonstrate these congenital anomalies with far greater clarity than can anteroposterior and lateral views alone.

CLARENCE E. WEAVER, M.D.

Deformities of the Thoracic Spine as a Cause of Anginoid Pain. J. R. Smith and W. B. Kountz. Ann. Int. Med. **17:** 604–617, October 1942.

Fifteen patients with pain of dorsal root origin whose symptoms simulated those of angina pectoris were observed. The occurrence of pain on exertion, its occasional short duration, and partial relief by nitrites were suggestive of cardiac origin. The majority of the patients described sharp pains in the back or chest but the choking or strangling sensations of true anginal pain were characteristically absent.

In all the cases reported, the roentgen-ray films showed only moderate osteo-arthritis, chiefly lipping and spurring in the four lower cervical vertebrae and the upper three or four dorsal vertebrae. It is probable that pathological changes about the intervertebral foramen, not easily seen even in detail films, may be responsible for severe symptoms.

More significant than x-ray studies were postural defects, which were evident in all of the patients of the group and were attributable to disease of the vertebral column. In some, straightening and stiffening of the dorsal spinal segment with limitation of movement, and in others, dorsal kyphosis of varying degree and markedly decreased movement of spine were present. Such defects are extremely common. Even when they are advanced, they may be asymptomatic.

The mechanism by which dorsal root stimulation is produced by hypertrophic spondylitis or other spinal deformity has not been satisfactorily explained. In order to throw light on this problem an experimental study was made on a cadaver with the spinal cord and nerves exposed, abnormal degrees of spinal flexion and extension being produced. When the spine was either flexed or straightened to an abnormal degree, the spinal canal tended to become elongated, so that the cord was drawn cephalad. This imposed tension on the spinal nerves, particularly at their angulations through the spinal foramina and at their attachments to the cord. It was postulated, then, that movement imposed on the nerves under such tension may give rise to irritation of the fibers, with production of referred pain, simulating angina pectoris.

STEPHEN N. TAGER, M.D.

Metabolic Studies on Neoplasm of Bone with the Aid of Radioactive Strontium. A. deG. Treadwell, B. V. A. Low-Beer, H. L. Friedell, and J. H. Lawrence. Am. J. M. Sc. **204:** 521–530, October 1942.

Chemical and spectrographic studies regarding the mineral composition of the animal body have revealed the presence of "trace" amounts of strontium in living tissue. Growing animals which were maintained on a diet low in calcium and in which the normal calcium requirement was replaced by strontium developed toxic symptoms clinically resembling rickets. The strontium-fed animals showed a considerably higher amount of water-soluble alkaline earth content in the bones than is found in rickets, and therefore a biochemical difference between the two elements was apparently demonstrated. It has been pointed out that strontium cannot replace calcium in normal bone formation.

By means of radioactive calcium and radioactive strontium, Pecher has found the following:

1. Of a dose of radioactive calcium, 58 per cent was recovered from the skeletons of mice after twenty-four hours. Of a dose of radioactive strontium, 33 per cent was similarly recovered.

2. In the case of both radioactive calcium and radioactive strontium the activity of the skeletons of mice indicated that nearly maximum uptake was reached eight hours after intravenous administration.

3. Bone uptake of the radioactive elements was nearly three times as great following intravenous administration as following oral administration.

4. Radioactive calcium or strontium originally fixed in the skeletons of mice was found to migrate to the fetuses during the last days of pregnancy and to be transferred to offspring through lactation.

5. Radioactive strontium administered intravenously to lactating cows was recovered in the milk in the amount of about 10 per cent of the dose during the first 4 1/2 days following administration.

In many cases the high phosphatase activity of osteogenic tumors is reflected in elevated serum phosphatase values. The inactivation of these tumors by external irradiation results in lowering the phosphatase activity of both the tumor tissue and the serum. These facts, together with the demonstrated reduction of serum phosphatase by the administration of radioactive strontium in one case suggested the possibility of a high uptake of strontium by osteogenic tumor tissue. Accordingly, small doses of radioactive strontium have been administered in 6 such cases, prior to biopsy or amputation, and the tissues have been assayed to determine uptake.

There is ample evidence that the maximum uptake of radio-strontium occurs in bone and tumor tissue. In soft tissues variation is especially noticeable, but a somewhat striking concentration is observed in several of the cases in the skin. Different parts of the tumor show marked differences in the uptake of strontium. This might be due, apart from causes such as vascularization, regressive local changes, and so on, to difference in the metabolic rate in different parts of the tumor depending on the state of cell development at the time of biopsy. The high uptake of strontium in areas where new bone is being laid down, whether this be normal or neoplastic, indicates that radioactive strontium will provide a valuable tool in the study of bone healing after experimental fractures.

Radio-strontium emits beta rays. Its half life is 55 days and its mean average life is 79.6 days. One microcurie of radio-strontium yields 38 r units daily per gram of tissue, assuming uniform distribution. Since strontium is taken up mainly by the osseous tissues, the radiation is concentrated chiefly in bones and osteogenic tissues.

In view of the exceedingly bad prognosis in cases of osteogenic tumors, and because of the known high resistance of these tumors to radiation, experience may prove that radio-strontium has therapeutic value chiefly as an adjunct to external radiation.

BENJAMIN COPLEMAN, M.D.

GYNECOLOGY AND OBSTETRICS

Problem of the "Tubal Sphincter" and of the Intramural Portion of the Fallopian Tube. P. Schneider. Am. J. Roentgenol. **48:** 527–542, October 1942.

Following filling with contrast fluid, the normal uterine cavity ordinarily appears in the roentgenogram as a triangular or approximately triangular shadow. From the upper angles of this triangle arise the shadows representing the tubal canals, at first thread-like, then, farther out, of greater caliber. In a large number of cases the continuity of the shadow near the origin of the tube at the uterine horn is either narrowed or completely interrupted. In discussions of this phenomenon, it has been designated definitely as "tubal sphincter" or less definitely as "sphincter-like muscular apparatus."

The author examined 22 uteri which had been removed at operation from women varying in age between thirty-five and fifty-two years. These were examined roentgenoscopically, usually within an hour after operation. In every instance a shadow-narrowing phenomenon was recognizable. In most cases the phenomenon was more or less distinctly visible, not always equally marked on the two sides. It was occasionally unilateral.

Studies were also made of specimens fixed in formalin solution. Anatomical-histological examination revealed that the shadow-narrowing phenomenon is produced by a folding of the mucous membrane of the corpus uteri. There is no sphincteric contraction nor indeed any muscular contraction at all. The situation is established at the boundary between the uterine cavity and the tube. The problem as to where the portion of the shadow lateral to the constriction phenomenon belongs is anatomically clarified by the

identification of this part as a dilated portion of the pars intramuralis of the tube.

For the occurrence of the mucosal folds two prerequisites seem important: (1) dilatation of the uterine cavity and some pressure upon the mucous membrane; (2) a certain degree of thickness of the mucous membrane. Very low pressures suffice to produce fold formation. The part of the pars intramuralis immediately adjacent to the uterine cavity is worthy of designation by a special name. The designation "antrum tubae" would seem logical from the anatomical point of view and, from the functional point of view, in accordance with the concept of a current directed from the uterus toward the abdominal cavity. This would represent that medial portion of the pars intramuralis which, characterized by its distensibility, is delimited medially by the above described fold formation, and laterally by that point of the tube which is not distensible. CLARENCE E. WEAVER, M.D.

THE GENITO-URINARY TRACT

Prostatic Abscess with Particular Reference to the Use of the Urethrogram in Diagnosis. W. E. Forsythe, Urol. & Cutan. Rev. **46:** 613–617, October 1942.

Prostatic abscesses are generally associated with urethral strictures, urethritis, and prostatitis; occasionally they follow urethral instrumentation. Metastatic abscesses of the prostate may occur as a complication of typhoid fever, influenza, measles, mumps, pneumonia, carbuncles, furuncles, and occasionally diabetes mellitus. Occasionally abscesses are seen with prostatic hyperplasia or carcinoma.

There is often no pre-existing prostatitis in the presence of an abscess. In these cases an embolus lodges in a prostatic vessel, sets up a secondary inflammation, which obstructs the tubules and results in a localized abscess. Small abscesses may coalesce to form a large solitary abscess.

The chief symptoms of prostatic abscesses are perineal, subpubic, or penile pain and difficulty in urination. Infrequently observed are fever, chill, malaise, and loss of weight.

Urethrography has been found very helpful in diagnosis, and the technic is briefly described. It includes the following steps: (1) routine preparation of the patient; (2) antero-posterior flat film; (3) removal of bladder contents by means of catheter; (4) placement of patient in oblique position with 45° flexion of lower thigh and extension of upper thigh; (5) centering of tube over symphysis pubis; (6) second film with bladder full of air; (7) removal of catheter, digital pressure being maintained on end of penile urethra in order to retain air, and slow injection of 20 c.c. of hippuran jelly mixture; (8) third film.

In the presence of a prostatic abscess the posterior urethra is narrowed, elongated, and appears rigid. The mid-portion is frequently deflected anteriorly and at the same time there is posterior deflection of the urethra at the vesical outlet. In aggravated cases the deflection may be S-shaped. This is interpreted as urethral distortion caused by the prostatic abscess. If there is an open communication between the abscess and the posterior urethra the abscess cavity will be outlined by the contrast medium. In carcinoma of the prostate the posterior urethra is narrowed and elongated, but there is little or no deflection of the urethra.

The author reports four cases.

MAURICE D. SACHS, M.D.

Pyelography in Perinephritic Abscess. E. Rioseco G., Urol. & Cutan. Rev. **46:** 629–630, October 1942.

Diagnosis of early perinephritic abscess is difficult. Gastro-intestinal distress is the chief complaint. This lasts about two months. Later the patient may complain of lumbar fossa pain. Careful questioning often elicits a history of a suppurative process in the tonsils, teeth, or skin.

Various methods of pyelography are discussed. To determine renal mobility the author takes one film of the abdomen in inspiration and a second in expiration. The distances between the centers of the pelves are measured. When a perinephritic abscess is present, the distance between the pelves increases during expiration, due to the ascent of the normal kidney. One case is reported with surgical confirmation.

MAURICE D. SACHS, M.D.

RADIOTHERAPY

Contact Roentgen Therapy. Evaluation of Results from a Clinical and Pathological Standpoint. W. E. Howes and M. R. Camiel. Am. J. Roentgenol. **48:** 360–376, September 1942.

Contact therapy finds its chief application in (1) lesions at or near the surface, with limited infiltration; (2) lesions in the accessible body cavities; (3) tumors which can be exposed surgically, such as those in the bladder or stomach. When the area to be treated is more than 2.4 cm. in diameter (the size of the tube head), multiple portals are employed.

This method of therapy has the advantage of convenience, speed, and economy. A basal-cell carcinoma may be adequately treated in from thirty to sixty seconds. Formerly inaccessible lesions and lesions near important structures can be treated because of the small size of the tube and the rapid drop in the intensity, since most of the rays are absorbed in the first few millimeters of tissue. This also permits eradication of the tumor without injury to the tumor bed. Cosmetic results are good.

The authors report a series of 100 cases. Practically all the patients were treated with 45 kv., 2 ma., 1.8-cm. target-skin distance, and no filter. With these factors the output was between 10,000 and 13,000 r per minute. For surface cauterization a dose of 10,000 r is used at one sitting, except for lesions lying on cartilage, where 5,000 to 6,000 r are given.

Limitations of the method, a description of the apparatus, the physical factors, the histopathology, the positioning of the patient, and details of the 100 cases treated are included, with numerous excellent illustrations.

This article should be read *in toto;* it is a complete course in this method of therapy.

S. M. ATKINS, M.D.

Roentgen Diagnosis and Treatment of Primary Pulmonary Neoplasm. George W. Holmes. Am. J. Roentgenol. **48:** 425–432, October 1942.

A diagnosis of primary carcinoma of the lung was made and confirmed by microscopic examination in 155 cases. These are divided into four groups—epidermoid carcinoma, 58 per cent; adenocarcinoma, 14.5 per cent; "oat-cell" carcinoma, 18.7 per cent; undifferentiated carcinoma, 8.4 per cent. Eighty per cent of the patients were males. Duration of symptoms was usually a matter of months rather than years.

Roentgen signs are the result of varying degrees of bronchial obstruction. When the tumor arises in one of the smaller bronchi, rounded or lobulated masses may be seen at a considerable distance from the hilum. Careful roentgenoscopic study of the chest is emphasized. By this method one may note lateral movement of the mediastinum, delayed or irregular movements of the diaphragm, fixations of the diaphragm, and abnormalities of the heart beat. Routine stereoscopic films of the chest may be wholly inadequate. Films should be taken during full inspiration, full expiration, and in the lateral view. Potter-Bucky diaphragm exposures may be necessary. It is sometimes necessary to resort to the planigraph or to the injection of opaque media. Bronchoscopy is of great value, especially in determining the exact nature of the lesion. The roentgenologist has done his part if he can state that an obstructing lesion of the bronchi is present and localize it accurately.

Benign adenomata are usually in a main stem bronchus, never in the smaller bronchi. The history is one of repeated attacks of bronchial obstruction over a long period of time. The end-results of treatment in this group show 89.2 per cent living and well, while in the group classified as malignant adenomata the survival rate was only 8.7 per cent. Irradiation is of little or no value in these benign cases. Surgical removal is the treatment of choice.

Adenocarcinoma often manifests itself by the appearance of a tumor at a varying distance from the primary tumor: either a dense rounded or lobulated mass close to the affected bronchus seen on the roentgen film or clinical evidence of metastases in the brain or other distant organ. Epidermoid carcinoma presents no characteristic roentgen findings, the picture being the classical one of bronchial carcinoma. "Oat-cell" carcinoma and undifferentiated carcinoma respond well to irradiation, and none has been benefited by surgical treatment. Not infrequently the appearance on the roentgenogram is that of a dense mass with a halo of fine line-like shadows extending into the surrounding tissues resembling somewhat the radiating lines seen in some malignant tumors of bone. The signs of bronchial obstruction may be absent.

Radiation Treatment: The use of radium has been discontinued in the author's clinic in the treatment of carcinoma of the bronchus. It is possible with supervoltage roentgen rays to cause a complete disappearance of the primary tumor in selected cases without serious injury to the surrounding tissues. Rather large doses, up to 5,000 or 6,000 r, given through a small field carefully centered over the primary tumor, will often relieve the bronchial obstruction and establish drainage. In no case is it justifiable to give heavy irradiation to large areas of infected lung tissues. Malignant adenomata and epidermoid carcinoma are radioresistant, but palliative results have been obtained. Treatment by irradiation gives the best palliative results in the "oat-cell" and other highly malignant tumors, and at the present time should be the method of choice. In large radiosensitive tumors the daily dose, especially in the early stage of this treatment, should not be too great.

If a primary neoplasm is discovered early, and there is a reasonable chance of cure, the author believes that surgery offers the best possibility of a five-year survival.

CLARENCE E. WEAVER, M.D.